§3 Age-structured models

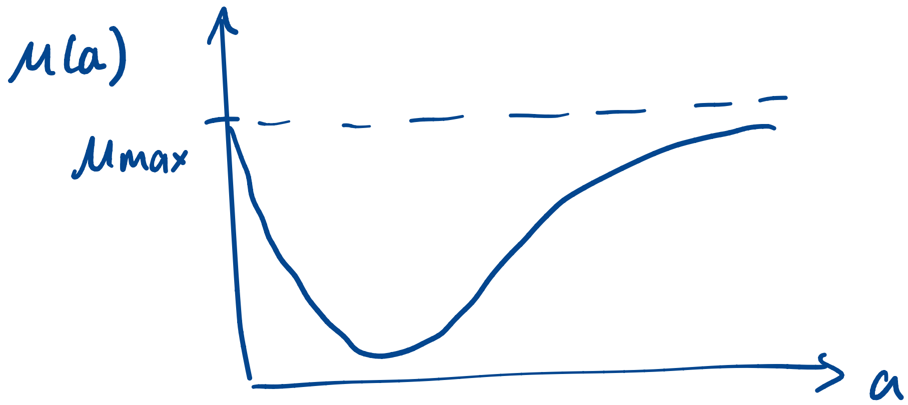
3.1 Simple age-structured models

$n(t, a)$ — number of individuals at age a at time t.

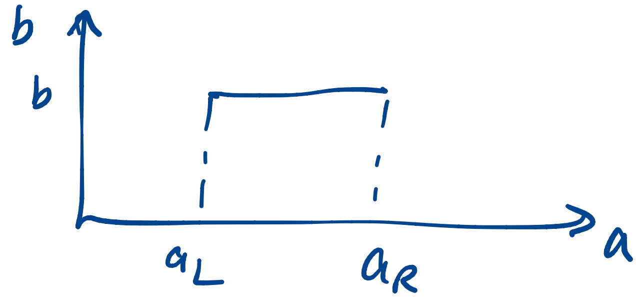
$b(a)$ — birth rate $\qquad \mu(a)$ — death rate

Examples:

$$\mu(a) = \mu_{max}\left(1 - \frac{A_{min}\, a}{A_{min}^2 + a^2}\right)$$



$$b(a) = \begin{cases} b & a_L < a < a_R \\ 0 & \text{o/w} \end{cases}$$



Von Foerster's Equation

- births contribute to $n(t,0)$
- over time δt 1. ageing
  2. death

$$dn(t,a) = \frac{\partial n}{\partial t}\delta t + \frac{\partial n}{\partial a}\delta a = -\mu(a)\, n(t,a)\,\delta t \qquad (*)$$

Divide by δt, note

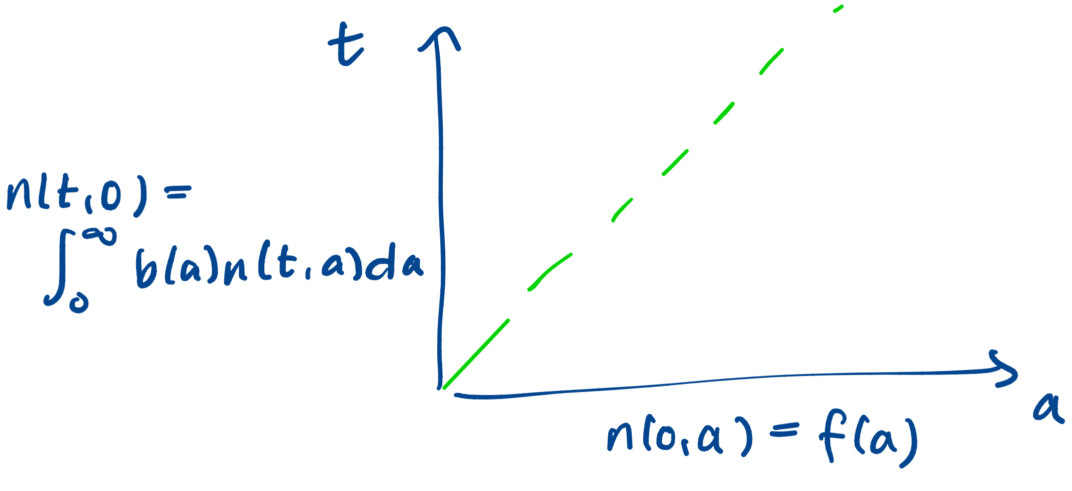
$$\lim_{\delta t \to 0} \frac{\delta a}{\delta t} = \frac{da}{dt} = 1$$

(*) Becomes $$\boxed{\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} = -\mu(a)\, n(t,a)}$$

Initial and boundary conditions:

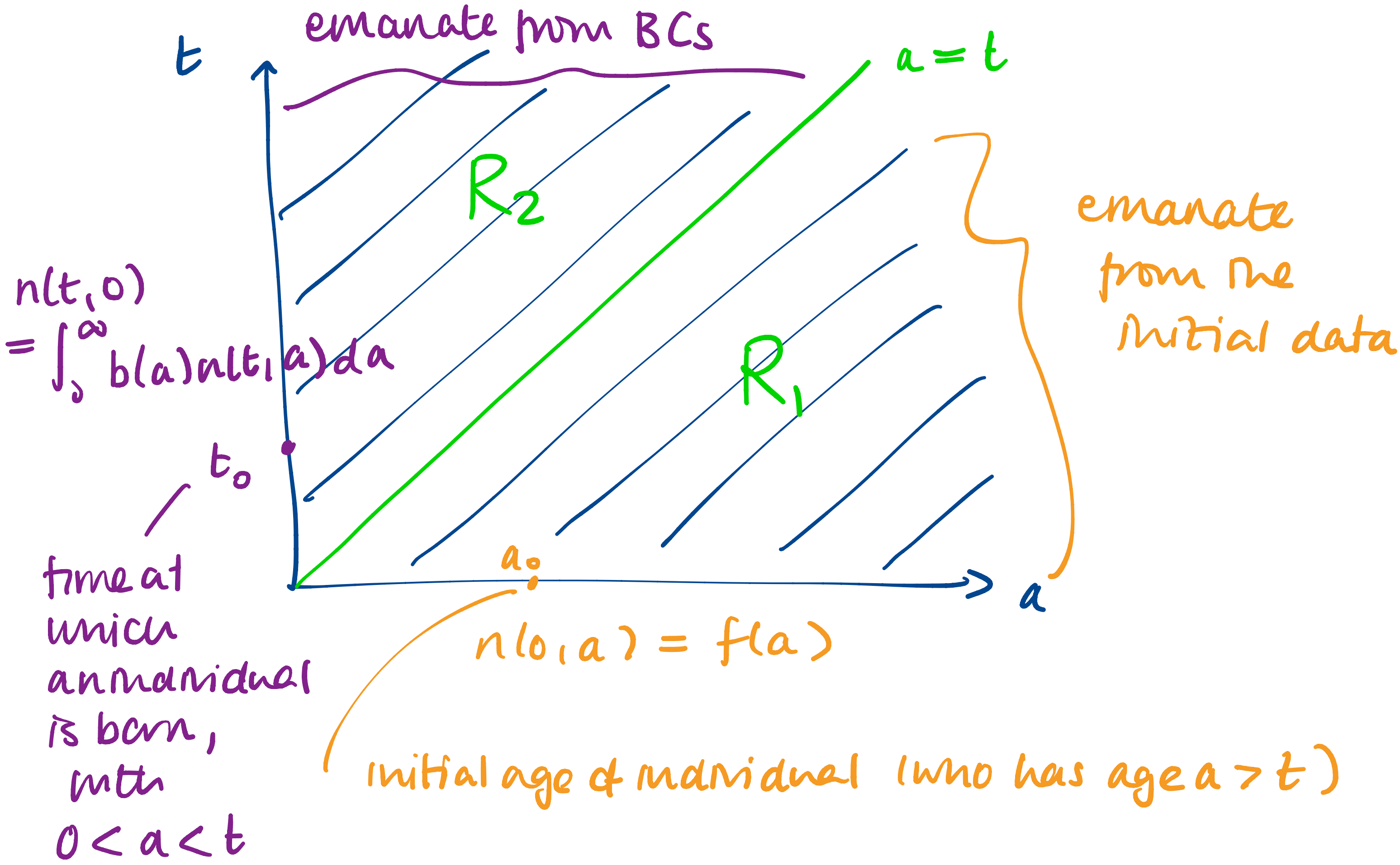
$$n(t,0) = \int_0^\infty b(a)\, n(t,a)\, da \qquad \text{total birth rate}$$

$$n(0,a) = f(a) \qquad \text{initial age distribution}$$



Method of Characteristics

characteristic curves: $\dfrac{da}{dt} = 1$, where $\dfrac{dn}{dt} = -\mu n$



characteristics: $a = \begin{cases} t + a_0 & a > t \\ t - t_0 & a < t \end{cases}$

REGION 1

$$\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} = -\mu(a)n \qquad n(0,a) = f(a)$$

characteristics: $a = t + a_0$

$$\frac{dn}{dt} = -\mu(t+a_0)n \qquad n(0,a_0) = f(a_0)$$

$$n(t,a) = \underbrace{n(0,a_0)}_{f(a_0)} e^{-\int_{a_0}^{a} \mu(\theta)\,d\theta}$$

Along characteristics: $a_0 = a - t$

$$n(t,a) = f(a-t)\, e^{\int_{a-t}^{a} \mu(\theta)\, d\theta}$$

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<u>REGION 2</u>

$$\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} = -\mu(a)\, n$$

$$n(t,0) = \int_0^\infty b(a)\, n(t,a)\, da.$$

Characteristics: $a = t - t_0$

$$\frac{dn}{dt} = -\mu(a)\, n = -\mu(t-t_0)\, n$$

$$n(t,a) = n(t_0, 0)\, e^{-\int_0^a \mu(\theta)\, d\theta}$$

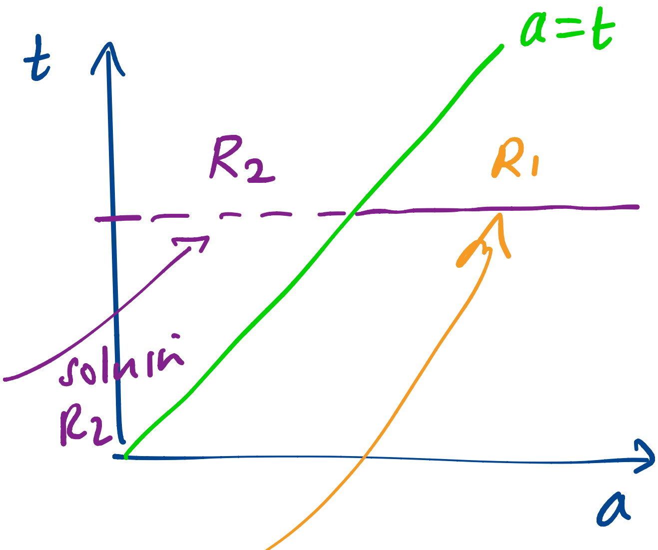
$$= n(t-a, 0)\, e^{-\int_0^a \mu(\theta)\, d\theta}$$

Using the BC:

$$n(t,0) = \int_0^\infty b(a)\, n(t,a)\, da$$

$$= \boxed{\int_0^t b(a)\, n(t,a)\, da}$$

$$+ \boxed{\int_t^\infty b(a)\, n(t,a)\, da}$$



soln in R_1

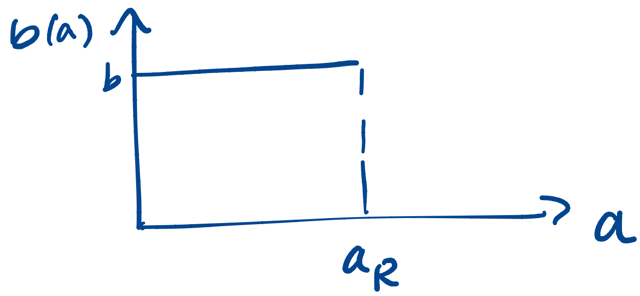
$$n(t,0) = \int_0^t \left[b(a)\, n(t-a,0)\, e^{-\int_0^a \mu(\theta)\,d\theta} \right] da$$

$$+ \int_t^\infty \left[b(a)\, f(a-t)\, e^{-\int_{a-t}^a \mu(\theta)\,d\theta} \right] da$$

linear eqn for $n(t,0)$.

Example

$$\mu(a) = \mu \quad , \quad b(a) = b\,H(a_R - a)$$

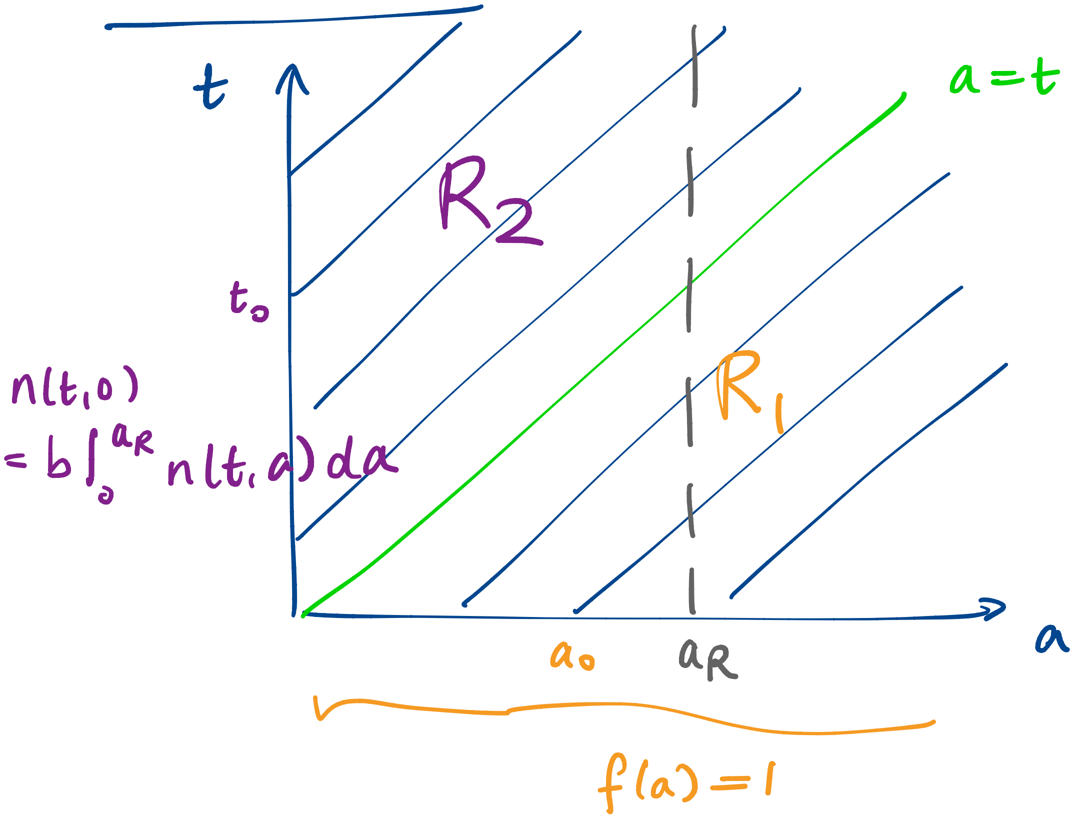


$$\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} = -\mu n \qquad n(0,a) = 1$$

$$n(t,0) = \int_0^\infty b(a)\,n(t,a)\,da$$

$$= b\int_0^{a_R} n(t,a)\,da$$

characteristics



$$a = \begin{cases} t + a_0 & a > t \\ t - t_0 & a < t \end{cases}$$

REGION 1 $\quad a > t$

characteristics : $a = t + a_0$

$$\frac{dn}{dt} = -\mu n \Rightarrow n(t,a) = \underbrace{n(0,a_0)}_{= f(a_0) = 1} e^{-\mu t}$$

$$= e^{-\mu t}$$

REGION2 $\quad t > a$

characteristics : $a = t - t_0$

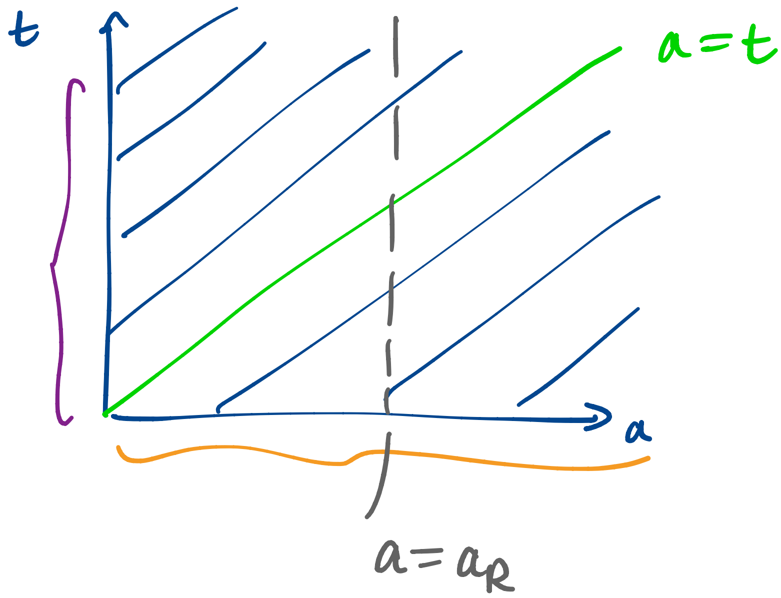
$$\frac{dn}{dt} = -\mu n \qquad n(t,0) = b\int_0^{a_R} n(t,a)\,da$$

$$\frac{d}{dt}\left(n(a,t)e^{\mu t}\right) = 0$$

$$n(t,a)e^{\mu t} - n(t_0,0)e^{\mu t_0} = 0$$

$$\Rightarrow \quad n(t,a) = n(t_0,0)e^{\mu(t_0-t)}$$

$$= n(t-a,0)e^{-\mu a}$$



Case 1: $t < a_R$

Case 2: $t > a_R$

<u>Case 1</u> $\quad 0 < t < a_R$

$$n(t,0) = b\int_0^{a_R} n(t,a)\,da$$

$$= b\int_0^t n(t,a)\,da + b\int_t^{a_R} n(t,a)\,da$$

$$= b\int_0^t n(t-a,0)e^{-\mu a}\,da + b\int_t^{a_R} e^{-\mu t}\,da$$

Let $N(t) = n(t,0)$

$$N(t) = b\underbrace{\int_0^t n(t-a,0)e^{-\mu a}\,da}_{} + b(a_R - t)e^{-\mu t}$$

$\tau = t - a$: $\quad da = -d\tau$

$0 \to t, \quad t \to 0$

$$= b\int_0^t N(\tau)e^{-\mu(t-\tau)}\,d\tau + b(a_R - t)e^{-\mu t}$$

differentiate

$$\frac{dN}{dt} = b\,N(t) - b\mu \int_0^t N(\tau) e^{-\mu(t-\tau)}\, d\tau$$
$$- \mu b (a_R - t) e^{-\mu t} - b e^{-\mu t}$$

μN

$$= (b-\mu) N - b e^{-\mu t}$$

$$\frac{d}{dt}\left(N(t) e^{-(b-\mu)t} \right) = - b e^{-bt}$$

$$N(t) e^{-(b-\mu)t} = \hat{N} + e^{-bt}$$

$$\boxed{N(t) = \hat{N} e^{(b-\mu)t} + e^{-\mu t}}$$

Substitute:

for $0 < t < a_R$

$$n(t,a) = \begin{cases} N(t-a) e^{-\mu a} & 0 < a < t \\ e^{-\mu t} & 0 < t < a \end{cases}$$

$$= \begin{cases} e^{-\mu t}\left[\hat{N} e^{b(t-a)} + 1\right] & 0 < a < t \\ e^{-\mu t} & 0 < t < a \end{cases}$$

Case 2 $\quad t > a_R$

$$N(t) = b\int_0^{a_R} N(t-a)\, e^{-\mu a}\, da$$

$\tau = t - a$

$d\tau = -da$

$0 \rightarrow t$

$a_R \rightarrow t - a_R$

$$= b\int_{t-a_R}^{t} N(\tau)\, e^{-\mu(t-\tau)}\, d\tau$$

differentiate:

$$\frac{dN}{dt} = bN(t) - bN(t-a_R)\, e^{-\mu(t-(t-a_R))} - \mu b\int_{t-a_R}^{t} N(\tau)\, e^{-\mu(t-\tau)}\, d\tau$$

$$= (b-\mu)N(t) - bN(t-a_R)\, e^{-\mu a_R}$$

$\Rightarrow$ delay differential eqn.

Seek solutions $\boxed{N(t) = \hat{N} e^{wt}}$

$$* \quad w = (b-\mu) - b\, e^{-(w+\mu)a_R}$$

Substitute:

$$n(t,a) = N(t-a)\, e^{-\mu a}$$

$$= \hat{N}\, e^{w(t-a)}\, e^{-\mu a}$$

$$N(t) = \tilde{N} e^{wt}$$

$Re(w) > 0 \Rightarrow$ popn grows

$Re(w) < 0 \Rightarrow$ popn decays

stable population : $w = 0$

$$b = \frac{\mu}{1 - e^{-\mu a_R}}$$

in this case : $n(t, a) = \begin{cases} e^{-\mu a} & 0 < a < t \\ e^{-\mu t} & a_R < t < a \end{cases}$

Notes

* $b > \mu$ for a stable population.
* $a_R \to \infty$ then $b \to \mu$ for a stable popn.
* $a_R \to 0$ then $b \to \frac{1}{a_R} \gg 1$ for a stable popn.

Separable solutions

$$n(t,a) = e^{\gamma t} F(a)$$

$F(a)$: stable age distribution

$e^{\gamma t}$:
growth $\mathrm{Re}(\gamma) > 0$
decline $\mathrm{Re}(\gamma) < 0$

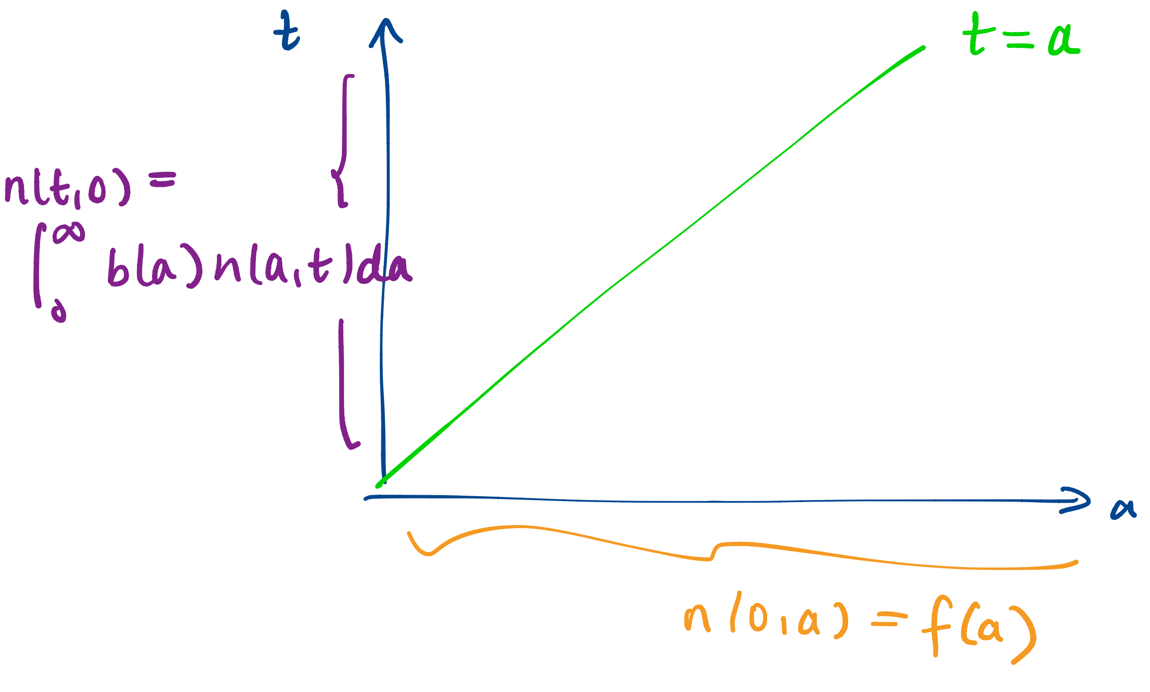
Population satisfies $\dfrac{\partial n}{\partial t} + \dfrac{\partial n}{\partial a} = -\mu(a) n$

Substitute : $\gamma e^{\gamma t} F(a) + e^{\gamma t} \dfrac{dF}{da} = -\mu(a) e^{\gamma t} F(a)$

$$\Rightarrow \quad \frac{dF}{da} = -(\mu(a) + \gamma) F$$

IF : $e^{\int_0^a \mu(\theta) d\theta + \gamma a}$

$$\Rightarrow \quad F(a) = F(0) e^{-\gamma a - \int_0^a \mu(\theta) d\theta}$$



$$n(t,0) = \int_0^\infty b(a)\, n(t,a)\, da$$

$$= \int_0^\infty b(a)\, e^{\gamma t} F(a)\, da$$

$$= e^{\gamma t} F(0) \int_0^\infty \left\{ b(a) e^{-\gamma a - \int_0^a \mu(\theta) d\theta} \right\} da$$

$$= e^{\gamma t} F(0) \quad \text{(by construction)}$$

equate and $e^{\gamma t} F(0)$:

$$1 = \int_0^\infty \left\{ b(a) e^{-\gamma a - \int_0^a \mu(\theta) d\theta} \right\} da := \Phi(\gamma) \quad (*_2)$$

Recall: $n(t,a) = e^{\gamma t} F(a)$

Note $\Phi(\gamma)$ is monotonic decreasing in γ

$\Rightarrow$ unique solution for γ

In general, a separable solution will not satisfy the initial conditions $n(0,a) = f(a)$.

$$n(t,0) \sim \int_0^t \left[b(a)\, n(t-a,0)\, e^{-\int_0^a \mu(\theta) d\theta} \right] da$$

↗ If we seek solutions of the form $n(t,a) = e^{\gamma t} F(a)$ the we will recover $(*_2)$.

3.2 Age-dependent epidemic models

Susceptibles – $S(t,a)$

Infectives – $I(t,a)$

infectiousness at age α

$$\frac{\partial S}{\partial t} + \frac{\partial S}{\partial a} = -\left(\int_0^\infty r(\alpha) I(t,\alpha)\,d\alpha\right) S(a,t) - \mu S(a,t)$$

$$\frac{\partial I}{\partial t} + \frac{\partial I}{\partial a} = +\underbrace{\left(\int_0^\infty r(\alpha) I(t,\alpha)\,d\alpha\right) S(a,t)}_{\text{infections}} - \underbrace{\mu I(a,t)}_{\text{natural death}}$$

Initial and boundary conditions

$$\underbrace{\begin{aligned} S(0,a) &= S_0(a) \\ I(0,a) &= I_0(a) \end{aligned}}_{\text{initial age profiles}} \qquad \begin{aligned} S(t,0) &= \int_0^\infty b(a) S(a,t)\,da \\ I(t,0) &= 0 \end{aligned}$$

infectives don't reproduce.

Separable solutions: $S(t,a) = e^{\gamma t} S(a)$

$I(t,a) = e^{\gamma t} I(a)$

In particular $\gamma = 0 \Rightarrow$ time-independent solutions.

$S(a), I(a)$

$$\frac{dS}{da} = -\left(\int_0^\infty r(\alpha) I(\alpha)\, d\alpha\right) S(a) - \mu S(a)$$

$$\frac{dI}{da} = +\left(\int_0^\infty r(\alpha) I(\alpha)\, d\alpha\right) S(a) - \mu I(a)$$

$$\frac{d}{da}(S+I) = -\mu(S+I) \Rightarrow \boxed{S(a)+I(a) = \Lambda e^{-\mu a}}$$

suppose $r(a) = r$, constant

$$\Rightarrow \frac{dI}{da} = r\underbrace{\left(\int_0^\infty I(\alpha)\, d\alpha\right)}_{I_{tot}} S(a) - \mu I(a)$$

$$= r I_{tot}\left[\Lambda e^{-\mu a} - I(a)\right] - \mu I(a)$$

$$= r I_{tot} \Lambda e^{-\mu a} - (\mu + r I_{tot}) I$$

$$\Rightarrow I(a) = A e^{-(\mu + r I_{tot})a} + \Lambda e^{-\mu a}$$

$$I_{tot} = \int_0^\infty I(\alpha)\, d\alpha$$

$$= \int_0^\infty \left(A e^{-(\mu + r I_{tot})a} + \Lambda e^{-\mu a}\right) da$$

$$= \frac{A}{\mu + r I_{tot}} + \frac{\Lambda}{\mu}$$

$$\Rightarrow \boxed{A = \left(I_{tot} - \frac{\Lambda}{\mu}\right)\left(\mu + r I_{tot}\right)}$$

$$I(a) = \left(I_{tot} - \frac{\Lambda}{\mu}\right)(\mu + rI_{tot})e^{-(\mu + rI_{tot})a} + \Lambda e^{-\mu a}$$

$$s(a) = \Lambda e^{-\mu a} - I(a)$$

$$= \left(\frac{\Lambda}{\mu} - I_{tot}\right)(\mu + rI_{tot})e^{-(\mu + rI_{tot})a}$$

To find I_{tot}, use the BC for s:

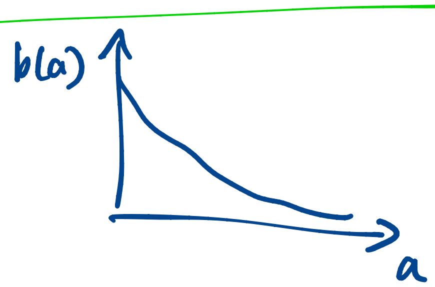
$$s(0) = \int_0^\infty b(a)\, s(a)\, da$$

$$\left(\frac{\Lambda}{\mu} - I_{tot}\right)\cancel{(\mu + rI_{tot})} = \left(\frac{\Lambda}{\mu} - I_{tot}\right)\cancel{(\mu + rI_{tot})} \times \int_0^\infty b(a) e^{-(\mu + rI_{tot})a}\, da$$

I_{tot} is determined as the solution of

$$\boxed{1 = \int_0^\infty b(a) e^{-(\mu + rI_{tot})a}\, da}$$

Suppose $b(a) = be^{-\theta a}$



Then $$1 = b\int_0^\infty e^{-(\mu + rI_{tot} + \theta)a}\, da = \frac{b}{\mu + rI_{tot} + \theta}$$

$$\Rightarrow \boxed{I_{tot} = \frac{b - \mu - \theta}{r}}$$

3.3 Structured models for populations of proliferating cells

Cell types: $p(t,s)$ = # cycling cells at position s of the cell cycle at time t.

$q(t,s)$ = # quiescent cells at position s of the cell cycle at time t.

$$\frac{\partial p}{\partial t} + \frac{\partial p}{\partial s} = -\mu N p - \Lambda N p + \frac{\delta q}{N_0 + N}$$

$$\frac{\partial q}{\partial t} = -\mu N q + \Lambda N p - \frac{\delta q}{N_0 + N}$$

cell death

cells exit the cell cycle

re-entry to the cell cycle.

length of cell cycle s.t. $0 \le s < T$.

$$N(t) = \int_0^T \big(p(t,s) + q(t,s)\big)\, ds$$ = total number of cells at time t.

Initial conditions

$p(0,s) = p_0(s)$

$q(0,s) = q_0(s)$

initial dist. of cell cycle phases.

Boundary condition

$p(t,0) = 2\,p(t,T)$

division at time T

Separable solutions : $\left.\begin{aligned} p(t,s) &= e^{\theta t} P(s) \\ q(t,s) &= e^{\theta t} Q(s) \end{aligned}\right\}$

with $\theta = 0$ so that population is constant.

$\Rightarrow N(t) = N$, constant.

$$\frac{dP}{ds} = -\mu N P - \lambda N P + \frac{\gamma \varphi}{N_0 + N} = -(\mu + \lambda) N P + \frac{\gamma \varphi}{N_0 + N}$$

$$\underbrace{0 = -\mu N \varphi + \lambda N P - \frac{\gamma \varphi}{N_0 + N}}$$

$$\Rightarrow \quad \varphi = \frac{\lambda N}{\mu N + \frac{\gamma \varphi}{N_0 + N}} \cdot P$$

$$= \left(\frac{\lambda N (N_0 + N)}{\mu N (N_0 + N) + \gamma} \right) P$$

$$\frac{1}{P}\frac{dP}{ds} = -\mu N \underbrace{\left(1 + \frac{\lambda N (N_0 + N)}{\mu N (N_0 + N) + \gamma} \right)}_{\text{constant}} = -w$$

$$P(s) = P_\infty e^{-ws}$$

$$\varphi(s) = \varphi_\infty e^{-ws} = \left(\frac{\lambda N (N_0 + N)}{\mu N (N_0 + N) + \gamma} \right) P_\infty e^{-ws}$$

The boundary condition gives

$$P(s=0) = 2P(s=T) \Rightarrow P_\infty = 2P_\infty e^{-wT}$$

$$\therefore \boxed{1 = 2e^{-wT}}$$

$$\Rightarrow \frac{\ln 2}{T} = w = \mu N \Bigg/ \left(1 + \frac{\lambda N(N_0+N)}{\mu N(N_0+N)+\gamma}\right)$$

$$N = \int_0^T [p(s)+\varphi(s)]\,ds$$

$$= \int_0^T [P_\infty + \varphi_\infty] e^{-ws}\,ds$$

$$= (P_\infty + \varphi_\infty)\left(\frac{1-e^{-wT}}{w}\right)$$

$e^{-wT} = \frac{1}{2}$

$$= \frac{P_\infty + \varphi_\infty}{2w}$$

$$\varphi_\infty = \frac{\lambda N(N_0+N)}{\gamma + \mu N(N_0+N)} P_\infty = \frac{w}{\mu N} - 1 \}$$

$$2wT = P_\infty\left[1 - \frac{w}{\mu N} - 1\right] = \frac{P_\infty w}{\mu N} \Rightarrow \boxed{P_\infty = 2\mu N^2}$$

$$P(s) = 2\mu N^2 e^{-ws}$$

$$\varphi(s) = 2\mu N^2\left(\frac{\lambda N(N_0+N)}{\gamma+\mu N(N_0+N)}\right)e^{-ws}$$