A kinetic theory of age-structured populations

Tom Chou (UCLA) and Chris Greenman (UEA)

SIAM DS17, May 22, 2017

Tracking objects with age

cells have cycles - division is not a Poisson process

molecular aging - mRNA polyadenylation

- RBCs marked for removal ($\sim$120 days)

age-dependent processes cannot be described using constant rates

Ideal theory would:

- keep track of ages
- model organism interactions (*e.g.*, carrying capacity)
- capture stochasticity

Organisms with internal “age”

A classic paradigm to track age in population biology:

- Lieut.-Col. A. G. M’Kendrick, *Applications of Mathematics to Medical Problems*, Proc. Edinburgh Math. Soc., **44**, 98–130, (1926)

- H. von Foerster, *Some remarks on changing populations*, in F. Stohlman, ed., *The kinetics of cell proliferation*, (1959)

Define:

- $\rho(a,t)\mathrm{d}a$: expected number with age in $(a, a+\mathrm{d}a)$
- $\beta(a)$: age-dependent birth rate
- $\mu(a)$: age-dependent death+emigration-immigration rate

McKendrick-von Foerster Equation

Integral equation derivation:

- $N(a,t) = \int_0^a \rho(y,t)\mathrm{d}y$: number with age in $(0,a)$
- $B(t) = \int_0^\infty \beta(y)\rho(y,t)\mathrm{d}y$: births/time, at t, from all particles
- $D(a,t) = \int_0^a \mu(y)\rho(y,t)\mathrm{d}y$: deaths/time of particles in age $(0,a)$

construct change in number

$$N(a+h,t+h) - N(a,t) = \int_t^{t+h} B(s)\mathrm{d}s - \int_0^h D(a+s,t+s)\mathrm{d}s$$

take $h \to 0$:

McKendrick-von Foerster Equation

$$\frac{\partial N(a,t)}{\partial t} + \frac{\partial N(a,t)}{\partial a} = \int_0^a \dot{\rho}(y,t)\mathrm{d}y + \rho(a,t) = B(t) - \int_0^a \mu(y)\rho(y,t)\mathrm{d}y$$

- McKendrick-von Foerster Eq. results from $\frac{\partial}{\partial a}$:

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

- “boundary condition” arises from setting $a = 0$:

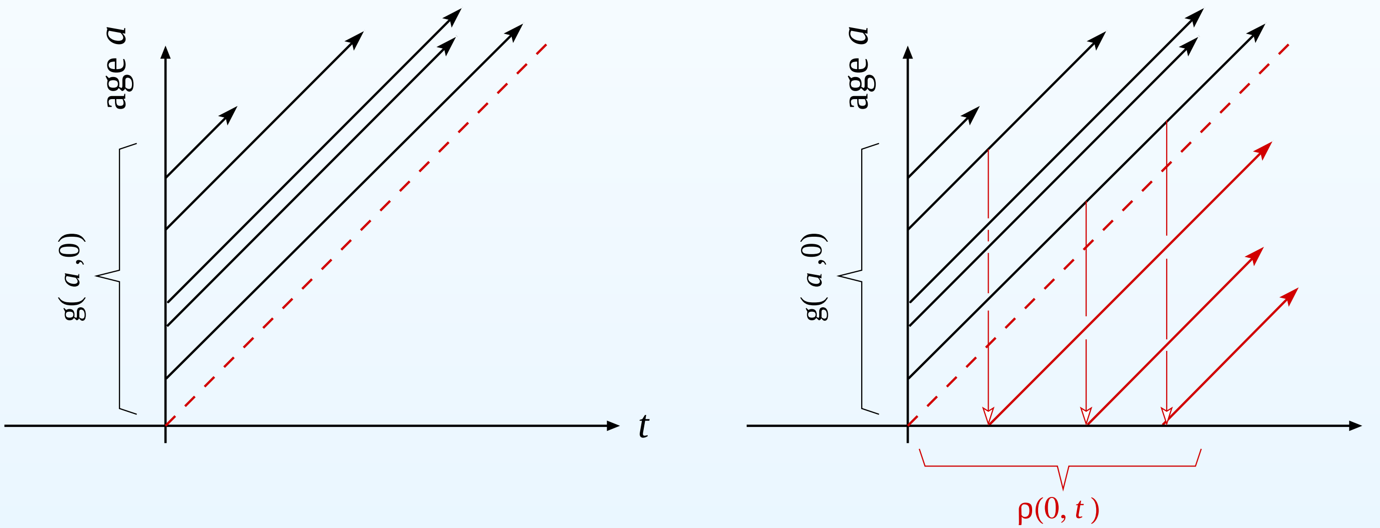
$$\rho(a=0,t) = \int_0^\infty \beta(a)\rho(a,t)\mathrm{d}a$$

$$\equiv B(t)$$ (birth rate of age zero particles)

- separately specify initial condition $\rho(a,0) \equiv g(a)$

Solution by characteristics

- characteristics: cohort at age a_0 at time t_0: $\frac{\mathrm{d}\bar{\rho}(h)}{\mathrm{d}h} + \bar{\mu}(h)\bar{\rho}(h) = 0$, where $\bar{\rho}(h) = \rho(a_0 + h, t_0 + h)$ and $\bar{\mu}(h) = \mu(a_0 + h)$



$$\rho(a,t) = \begin{cases} g(a-t)\exp\left[-\int_{a-t}^{a}\mu(s)\mathrm{d}s\right], & a \geq t. \\ \underbrace{B(t-a)}_{\text{depends on } \rho}\ \exp\left[-\int_{0}^{a}\mu(s)\mathrm{d}s\right], & a < t. \end{cases}$$

Interactions?

- $\rho(a > t, t) = g(a - t) \exp\left[-\int_0^t \mu(a - t + h'; n(h'))\mathrm{d}h'\right]$
- $\rho(a < t, t) = \rho(0, t - a) \exp\left[-\int_0^a \mu(h'; n(t - a + h'))\mathrm{d}h'\right]$

$$= B(t - a; n(t - a)) \exp\left[-\int_0^a \mu(h'; n(t - a + h'))\mathrm{d}h'\right]$$

self-consistently solve using $n(t) = \int_0^\infty \rho(a, t)\mathrm{d}a$

- However, McKendrick-von Foerster equations are still *deterministic* and do not give probability distributions

Stochastic descriptions

- Master eqn: *probability* $P_n(t)$ of exactly n particles at time t:

$$\frac{\partial P_n(t)}{\partial t} = \alpha_n(t)\left[P_{n-1} - P_n\right] + (n-1)\beta_{n-1}(t)P_{n-1} - n(\beta_n(t) + \mu_n(t))P_n + (n+1)\mu_{n+1}(t)P_{n+1}$$

ME assumes event times are *exponentially distributed*.
In the rates $\alpha_n(t), \beta_n(t)$, and $\mu_n(t)$, $t \equiv$ time, *not* age.

- hidden Markov states: requires many states

- age-binning: incompatible with large system-size expansion

- Bellman-Harris branching process: treats general waiting time distributions but assumes iid $\rightarrow$ no interactions

New kinetic description

- Extend ideas of kinetic theory to higher dimensions
- Interactions affect birth-death rates, but no “collision” terms
- Assume age-ordering of n *distinguishable* individuals and define

$$f_n(x_1, x_2, x_3, \ldots, x_n; t)\mathrm{d}x_1\mathrm{d}x_2 \ldots \mathrm{d}x_n \equiv f_n(\mathbf{x}_n; t)\mathrm{d}\mathbf{x}_n$$

probability that at time t, there are n distinguishable particles (*e.g.*, by birth time) with youngest within age $(x_1, x_1 + \mathrm{d}x_1)$, the second youngest within age $(x_2, x_2 + \mathrm{d}x_2)$, and so on.

High-dimensional kinetic theory

Next, define an ordered cumulative probability:

$$Q_n(\mathbf{a}_n;t) = \int_0^{a_1} \mathrm{d}x_1 \int_{x_1}^{a_2} \mathrm{d}x_2 \cdots \int_{x_{n-2}}^{a_{n-1}} \mathrm{d}x_{n-1} \int_{x_{n-1}}^{a_n} \mathrm{d}x_n f_n(x_1,\ldots,x_n;t),$$

where $\mathbf{a}_n = (a_1, a_2, \ldots, a_n)$.

Q is the probability that the youngest has age x_1 between 0 and a_1, the second youngest has age x_2 between x_1 and a_2, and so on.

High-dimensional kinetic theory

Compute the change in $Q_n(\mathbf{a}_n; t)$ over a small time increment:
$Q_n(\mathbf{a}_n + \boldsymbol{\varepsilon}; t + \varepsilon) = Q_n(\mathbf{a}_n; t) + \int_t^{t+\varepsilon} J(t')\mathrm{d}t'$. For $\varepsilon \to 0$:

$$\frac{\partial Q_n(\mathbf{a}_n; t)}{\partial t} + \sum_{i=1}^{n} \frac{\partial Q_n(\mathbf{a}_n; t)}{\partial a_i} = J^+(\mathbf{a}_n; t) - J^-(\mathbf{a}_n; t).$$

The probability fluxes can be decomposed into components representing birth (β) and death (μ):

$$J^{\pm}(\mathbf{a}_n; t) = J^{\pm}_{\beta}(\mathbf{a}_n; t) + J^{\pm}_{\mu}(\mathbf{a}_n; t).$$

$\pm$ represent terms that enter or leave state

Probability fluxes

$$J_\beta^-(\mathbf{a}_n;t) = \int_0^{a_1} \mathrm{d}x_1 \int_{x_1} \cdots \int_{x_{j-1}}^{a_j} \mathrm{d}x_j \cdots \int_{x_{n-1}}^{a_n} \mathrm{d}x_n \sum_{i=1}^{n} \beta_n(x_i) f_n(\mathbf{x}_n;t),$$

$$J_\mu^-(\mathbf{a}_n;t) = \int_0^{a_1} \mathrm{d}x_1 \cdots \int_{x_{j-1}}^{a_j} \mathrm{d}x_j \cdots \int_{x_{n-1}}^{a_n} \mathrm{d}x_n \sum_{i=1}^{n} \mu_n(x_i) f_n(\mathbf{x}_n;t),$$

$$J_\beta^+(\mathbf{a}_{2,n};t) = \int_0^{a_2} \mathrm{d}x_1 \cdots \int_{x_{j-1}}^{a_{j+1}} \mathrm{d}x_j \cdots \int_{x_{n-2}}^{a_n} \mathrm{d}x_{n-1} \sum_{i=1}^{n-1} \beta_{n-1}(x_i) f_{n-1}(\mathbf{x}_{n-1};t),$$

$$J_\mu^+(\mathbf{a}_n;t) = \sum_{j=0}^{n} \int_0^{a_1} \mathrm{d}x_1 \cdots \int_{x_{j-1}}^{a_j} \mathrm{d}x_j \int_{x_j}^{a_{j+1}} \mathrm{d}y \int_y^{a_{j+1}} \mathrm{d}x_{j+1} \cdots$$

$$\cdots \int_{x_{n-1}}^{a_n} \mathrm{d}x_n \, \mu_{n+1}(y) f_{n+1}(x_1,\ldots,x_j,y,x_{j+1},\ldots,x_n;t),$$

where $\mathbf{a}_{i,j} = (a_i, a_{i+1}, \ldots, a_j)$, $x_0 \equiv 0$, and $a_{n+1} \equiv \infty$.

Kinetic equations: indistinguishable particles

- for n *indistinguishable* particles, define $\rho_n(x_1, x_2, \ldots, x_n; t) = \frac{1}{n!} f_n(\mathbf{x}_n; t)$ as prob. first randomly chosen particle has age in $(x_1, x_1 + \mathrm{d}x_1)$, and so on.

- define $\gamma_n(a_i) \equiv \beta_n(a_i) + \mu_n(a_i)$ and apply $\frac{\partial}{\partial a_1}\frac{\partial}{\partial a_2}\cdots\frac{\partial}{\partial a_n}$:

$$\frac{\partial \rho_n(\mathbf{a}_n; t)}{\partial t} + \sum_{j=1}^{n} \frac{\partial \rho_n(\mathbf{a}_n; t)}{\partial a_j} = - \sum_{i=1}^{n} \gamma_n(a_i)\rho_n(\mathbf{a}_n; t) + (n+1)\int_0^\infty \mu_{n+1}(y)\rho_{n+1}(\mathbf{a}_n, y; t)\mathrm{d}y$$

- set $a_\ell = 0$ and take $\frac{\partial}{\partial a_1}\cdots/\cdots\frac{\partial}{\partial a_n}$. BCs:

$$n\rho_n(a_1, \ldots, a_\ell = 0, \ldots, a_n; t) = \sum_{i=1}^{n}{}' \beta_{n-1}(a_i)\rho_{n-1}(a_1, \ldots, \hat{a}_\ell, \ldots, a_n; t)$$

Equation hierarchies

Reduced dist: $\int_0^\infty \mathrm{d}a_{k+1} \ldots \int_0^\infty \mathrm{d}a_n \, \rho_n(\mathbf{a}_n; t) \equiv \rho_n^{(k)}(\mathbf{a}_k; t)$

Integrating Eqs. for $\rho(\mathbf{a}_n; t)$ over $n-k$ ages and BC over $n-k-1$ ages, kinetic equation becomes

$$\begin{aligned}
\frac{\partial \rho_n^{(k)}(\mathbf{a}_k;t)}{\partial t} + \sum_{i=1}^{k} \frac{\partial \rho_n^{(k)}(\mathbf{a}_k;t)}{\partial a_i} = \quad & \left(\frac{n-k}{n}\right) \sum_{i=1}^{k} \beta_{n-1}(a_i) \rho_{n-1}^{(k)}(\mathbf{a}_k;t) \\
& + \frac{(n-k)(n-k-1)}{n} \int_0^\infty \beta_{n-1}(y) \rho_{n-1}^{(k+1)}(\mathbf{a}_k, y; t) \mathrm{d}y \\
& - \sum_{i=1}^{k} \gamma_n(a_i) \rho_n^{(k)}(\mathbf{a}_k;t) - (n-k) \int_0^\infty \gamma_n(y) \rho_n^{(k+1)}(\mathbf{a}_k, y; t) \\
& + (n+1) \int_0^\infty \mu_{n+1}(y) \rho_{n+1}^{(k+1)}(\mathbf{a}_k, y; t) \mathrm{d}y.
\end{aligned}$$

$\rho_n^{(k)}$ depends on $\rho_{n,n\pm1}^{(k+1)}$ $\Rightarrow$ equation hierarchy

Equation hierarchies

Reduced dist: $\int_0^\infty \mathrm{d}a_{k+1} \ldots \int_0^\infty \mathrm{d}a_n \, \rho_n(\mathbf{a}_n;t) \equiv \rho_n^{(k)}(\mathbf{a}_k;t)$

Integrating Eqs. for $\rho(\mathbf{a}_n;t)$ over $n-k$ ages and BC over $n-k-1$ ages, kinetic equation becomes

$$\begin{aligned}
\frac{\partial \rho_n^{(k)}(\mathbf{a}_k;t)}{\partial t} + \sum_{i=1}^{k} \frac{\partial \rho_n^{(k)}(\mathbf{a}_k;t)}{\partial a_i} = & \left(\frac{n-k}{n}\right) \sum_{i=1}^{k} \beta_{n-1}(a_i) \rho_{n-1}^{(k)}(\mathbf{a}_k;t) \\
& + \frac{(n-k)(n-k-1)}{n} \int_0^\infty \beta_{n-1}(y) \rho_{n-1}^{(k+1)}(\mathbf{a}_k, y; t) \mathrm{d}y \\
& - \sum_{i=1}^{k} \gamma_n(a_i) \rho_n^{(k)}(\mathbf{a}_k;t) - (n-k) \int_0^\infty \gamma_n(y) \rho_n^{(k+1)}(\mathbf{a}_k, y; t) \\
& + (n+1) \int_0^\infty \mu_{n+1}(y) \rho_{n+1}^{(k+1)}(\mathbf{a}_k, y; t) \mathrm{d}y.
\end{aligned}$$

$\rho_n^{(k)}$ depends on $\rho_{n,n\pm1}^{(k+1)} \Rightarrow$ equation hierarchy

Lowest-order ($k = 0$) equation

$$\frac{\partial \rho_n^{(0)}(t)}{\partial t} = (n-1)\int_0^\infty \beta_{n-1}(y)\rho_{n-1}^{(1)}(y;t)\mathrm{d}y - n\int_0^\infty \left[\beta_n(y)+\mu_n(y)\right]\rho_n^{(1)}(y;t)\mathrm{d}y + (n+1)\int_0^\infty \mu_{n+1}(y)\rho_{n+1}^{(1)}(y;t)\mathrm{d}y$$

If β_n and μ_n are age-independent,

$$\frac{\partial \rho_n^{(0)}(t)}{\partial t} = (n-1)\beta_{n-1}\rho_{n-1}^{(0)}(t) - n(\beta_n+\mu_n)\rho_n^{(0)}(t) + (n+1)\mu_{n+1}\rho_{n+1}^{(0)}(t),$$

$\Rightarrow$ hierarchy in birth-death master equation

Expected density

$$\rho(a;t) \equiv \sum_{n=0}^{\infty} n\rho_n^{(1)}(a;t) \quad \text{expected density}$$

Multiply $k = 1$ eqn by n and summing:

$$\begin{aligned}
\frac{\partial \rho(a;t)}{\partial t} + \frac{\partial \rho(a;t)}{\partial a} = \quad & \sum_{n=2}^{\infty} (n-1)\beta_{n-1}(a)\rho_{n-1}^{(1)}(a;t) \\
& + \sum_{n=3}^{\infty} (n-1)(n-2) \int_0^{\infty} \beta_{n-1}(y)\rho_{n-1}^{(2)}(a,y;t)\mathrm{d}y \\
& - \sum_{n=1}^{\infty} n\gamma_n(a)\rho_n^{(1)}(a;t) - \sum_{n=2}^{\infty} n(n-1) \int_0^{\infty} \gamma_n(y)\rho_n^{(2)}(a,y;t) \\
& + \sum_{n=1}^{\infty} n(n+1) \int_0^{\infty} \mu_{n+1}(y)\rho_{n+1}^{(2)}(a,y;t)\mathrm{d}y,
\end{aligned}$$

Deterministic limit

Eq. reduces to

$$\frac{\partial\rho(a;t)}{\partial t}+\frac{\partial\rho(a;t)}{\partial a}=-\sum_{n=1}^{\infty}\mu_n(a)n\rho_n^{(1)}(a;t)$$

Integrating all but one age in BC and summing over all n:

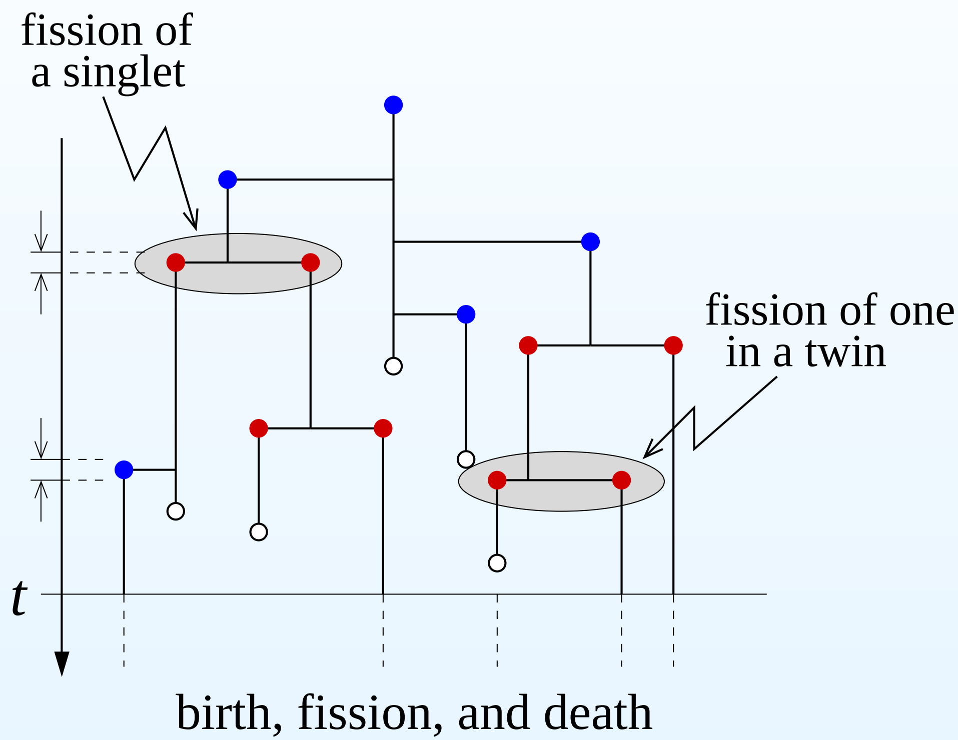
$$\sum_{n=1}^{\infty}n\rho_n^{(1)}(a=0;t)\equiv\rho(a=0;t)=\sum_{n=2}^{\infty}\int_0^{\infty}\beta_{n-1}(y)(n-1)\rho_{n-1}^{(1)}(y;t)\mathrm{d}y$$

MCK eqn recovered if $\mu(a)$ and $\beta(a)$ are n-independent

n-dependent $\beta_n(a), \mu_n(a) \Rightarrow$ hierarchy in MCK eqn

Generalization to fission-death process

Branching process = birth + immediate renewal of parent



Density function needs to consider *pairs* of particles.

Define densities according to time of birth (TOB): $\mathbf{x} = t - \mathbf{a}$; $\mathbf{y} = t - \mathbf{a}'$

Fission: indistinguishable particles

Density for $\rho_{m,n}(\mathbf{x}_m;\mathbf{y}_n) = \frac{1}{m!n!} f_{m,n}(\mathbf{x}_m;\mathbf{y}_n)$ for m unordered singlets with TOB in $[\mathbf{x}, \mathbf{x} + \mathrm{d}\mathbf{x})$ *and* n unordered pairs with TOB in $[\mathbf{y}, \mathbf{y} + \mathrm{d}\mathbf{y})$ obeys:

$$\frac{\partial \rho_{m,n}}{\partial t} + \rho_{m,n} \sum_{i=1}^{m} \left[\sum_{j=1}^{n} \beta_{m,n}(a_i, a'_j) + \mu_{m,n}(a_i) \right] =$$

$$(m+1) \int_{-\infty}^{t} \rho_{m+1,n}(\mathbf{x}_m, z; \mathbf{y}_n) \mu_{m+1,n}(t-z) \mathrm{d}z$$

$$+ 2 \left(\frac{m+1}{n} \right) \sum_{i=1}^{m} \rho_{m-1,n+1}(\mathbf{x}_{i-1}, \mathbf{x}_{i+1,m}; \mathbf{y}_n, x_i) \mu_{m-1,n+1}(t - x_i)$$

where BC's are $\rho_{m,n}(\mathbf{x}_{m-1}, t; \mathbf{y}) = 0$ and

$$\rho_{m,n}(\mathbf{x}_m; \mathbf{y}_{n-1}, t) = \frac{2}{m} \sum_{i=1}^{m} \rho_{m-1,n}(\mathbf{x}_{i-1}, \mathbf{x}_{i+1,m}; \mathbf{y}_{n-1}, x_i) \beta_{m-1,n}(t - x_i)$$

$$+ \left(\frac{m+1}{n} \right) \int_{-\infty}^{t} \rho_{m+1,n-1}(\mathbf{x}_m, z; \mathbf{y}_{n-1}) \beta_{m+1,n-1}(t-z) \mathrm{d}z$$

Fission-death process: reduced distribution

$$\rho_{m,n}^{(k,\ell)}(\mathbf{x}_k;\mathbf{y}_\ell;t) \equiv \int_{-\infty}^{t} \mathrm{d}\mathbf{x}'_{m-k} \int_{-\infty}^{t} \mathrm{d}\mathbf{y}'_{n-\ell}\,\rho_{m,n}(\mathbf{x}_k,\mathbf{x}'_{m-k};\mathbf{y}_\ell,\mathbf{y}'_{n-\ell};t)$$

obeys a double hierarchy

lowest order marginals:

$$X(x,t) \equiv \sum_{m,n=0}^{\infty} m\rho_{m,n}^{(1,0)}(x;;t) = \sum_{m,n=0}^{\infty} m \int_{-\infty}^{t} \mathrm{d}\mathbf{x}_{m-1} \int_{-\infty}^{t} \mathrm{d}\mathbf{y}_n\,\rho_{m,n}(\mathbf{x}_{m-1},x;\mathbf{y}_n;t)$$

$$Y(y,t) \equiv \sum_{m,n=0}^{\infty} n\rho_{m,n}^{(0,1)}(;y;t) = \sum_{m,n=0}^{\infty} n \int_{-\infty}^{t} \mathrm{d}\mathbf{x}_m \int_{-\infty}^{t} \mathrm{d}\mathbf{y}_{n-1}\,\rho_{m,n}(\mathbf{x}_m;\mathbf{y}_{n-1},y;t)$$

Fission-death: lowest order closure

If $\beta_{m,n}(a) = \beta(a)$ and $\mu_{m,n}(a) = \mu(a)$,

$$\frac{\partial X}{\partial t} = (2Y - X)\gamma(t-x), \qquad \frac{\partial Y}{\partial t} = -2Y\gamma(t-x)$$

Similarly, boundary conditions become:

$$X(t,t) = 0, \qquad Y(t,t) = \int_{-\infty}^{t} (X(z,t) + 2Y(z,t))\gamma(t-z)\mathrm{d}z \equiv B(t)$$

Total population density $T(x,t) = X(x,t) + 2Y(x,t)$ reduces to McKendrick-von Foerster-like equation:

$$\frac{\partial T}{\partial t} = -\gamma(t-z)T, \qquad T(t,t) = \int_{-\infty}^{t} T(z,t)\gamma(t-z)\mathrm{d}z$$

which can be formally solved...

Fission model (pure birth)

mean field limit of fission model w/ birth time dist: $g(t) = \frac{\alpha^\alpha t^{\alpha-1} e^{-\alpha t}}{\Gamma(\alpha)}$

as $\alpha \to \infty, g(t) \to \delta(t-1)$ (discrete-time Galton-Watson process)

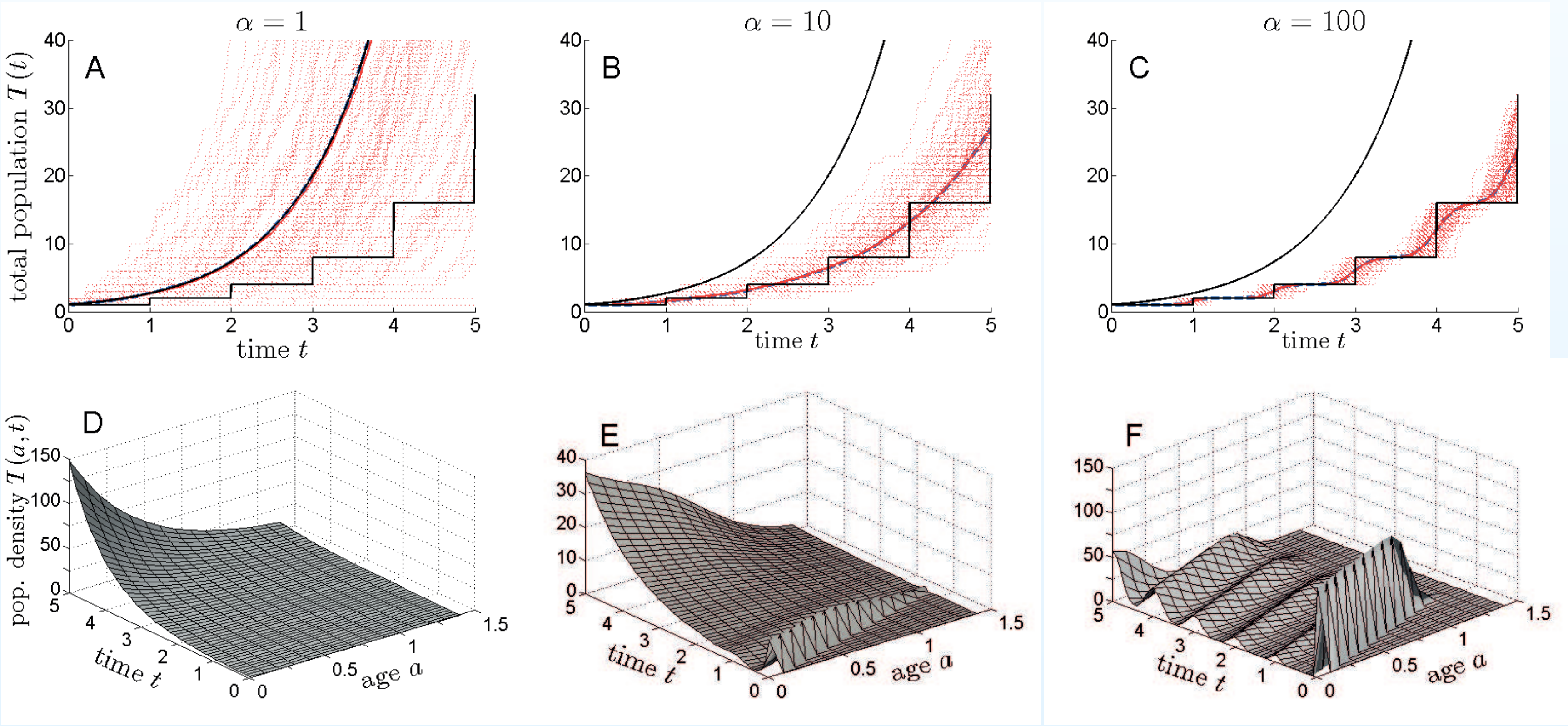


Table of pros and cons

Theory	stochastic	age-dep. rates	age-structured pop.	age-resolved	inter-actions	budding	fission
Logistic Eq.	✗	✗	✗	✗	✓	✗	✗
McKendrick	✗	✓	✓	✗	✓	✓	✗
Master Eq.	✓	✗	✗	✗	✓	✓	✓
Bellman-Harris	✓	✓	✗	✗	✗	✗	✓
Age bins	✗	✓	✓	✗	✓	✗	✗
Kinetic Theory	✓	✓	✓	✓	✓	✓	✓

Spatial dependence - simple diffusion

Define $\hat{\rho}_n(\mathbf{b}_n; \mathbf{q}_n; t)$: density for a population containing n randomly labelled individuals with TOBs $\mathbf{b}_n$ *and* positions $\mathbf{q}_n$

$\hat{\rho}_n(\mathbf{b}_n; \mathbf{q}_n; t)$ is invariant under particle permutations, but relative orders of $\mathbf{b}_n$ and $\mathbf{q}_n$ must be preserved: $\hat{\rho}_2(b_1, b_2; q_1, q_2; t) = \hat{\rho}_2(b_2, b_1; q_2, q_1; t)$

$$\frac{\partial \hat{\rho}_n(\mathbf{b}_n; \mathbf{q}_n; t)}{\partial t} = -\,\hat{\rho}_n(\mathbf{b}_n; \mathbf{q}_n; t) \sum_{i=1}^{n} \gamma_n(t - b_i, q_i) + D \sum_{i=1}^{n} \frac{\partial^2}{\partial q_i^2} \hat{\rho}_n(\mathbf{b}_n; \mathbf{q}_n; t)$$
$$+ (n+1) \int_{-\infty}^{t} \mathrm{d}y \int_{\mathbb{R}} \mathrm{d}q' \; \hat{\rho}_{n+1}(\mathbf{b}_n, y; \mathbf{q}_n, q'; t) \mu_{n+1}(t - y, z).$$

boundary condition

$$\rho_n(\mathbf{b}_{n-1}, t; \mathbf{q}_n; t) = \frac{1}{n} \sum_{i=1}^{n-1} \rho_{n-1}(\mathbf{b}_{n-1}; \mathbf{q}_{n-1}; t) \beta(t - b_i, q_i) \delta(q_n - q_i),$$

Spatial dependence: formal solution

$$\frac{\partial}{\partial t}\left[U_n^{-1}(\mathbf{b}_n;\mathbf{q}_n;t_0,t)\rho_n\right] = D\sum_{j=1}^{n}\frac{\partial^2}{\partial q_j^2}\left[U_n^{-1}\rho_n\right] + (n+1)U_n^{-1}\int_{-\infty}^{t}\mathrm{d}y\int_{\mathbb{R}}\mathrm{d}z\ \rho_{n+1}(\mathbf{b}_n,y;\mathbf{q}_n,z;t)\mu_{n+1}(t-y,z),$$

where

$$U_n(\mathbf{b}_n;\mathbf{q}_n;t_0,t) = \exp\left[-\sum_{i=1}^{n}\int_{t_0}^{t}\gamma_n(s-b_i,q_i)\mathrm{d}s\right]$$

Summary & Conclusions

- Developed a new fully stochastic age-structured theory
- Kinetic theory for marginal densities leads to BBGKY hierarchy
- Theory handles both age- and population-dependent processes
- Branching/fission processes requires additional n dimensions: $\rho_{m,n}(\mathbf{x}_m; \mathbf{y}_n; t)$ and double hierarchy
- Generalizes McKendrick eqn to fission
- Spatial dynamics easily incorporated
- Many limiting analytic and asymptotic solutions accessible

More details in:

Greenman and Chou, PRE, **93**, 012112, (2016)

Chou and Greenman, J. Stat. Phys., **164**, 49-76, (2016)

Kinetic solutions: simplifying cases

- pure death ($\beta = 0$): $t_0 = 0$, $\rho_n(\mathbf{a}_n - t; 0) = \rho(n) \prod_{i=1}^{n} g(a_i - t)$, and $\mu_n(a) = \mu(a)$:

$$\rho_n(\mathbf{a}_n; t) = U(\mathbf{a}_n; 0; t) \prod_{i=1}^{n} g(a_i - t) \sum_{k=0}^{\infty} \binom{n+k}{k} \rho(n+k) \left[\int_0^t g(y-s) \int_s^{\infty} U(y; 0; s)\mu(y) \mathrm{d}y \mathrm{d}s \right]^k$$

- pure birth ($\mu = 0$). Use birth BC and use $U(\mathbf{a}_n; 0; t)$ between births: $\rho_n(\mathbf{a}_n; t) = \frac{1}{n} U_n(\mathbf{a}_n; b_n; t) \rho_{n-1}(\mathbf{a}_{n-1} - a_n; t - a_n) \sum_{i=1}^{n-1} \beta_{n-1}(a_i - a_n)$. Assuming $\beta_n(a) = \beta(a)$, chose $t_0 > b_i$ and iterate back in time:

$$\rho_n(\mathbf{a}_n; t) = g_m(\mathbf{a}_m - t) U(\mathbf{a}_m; 0; t) \frac{m!}{n!} \prod_{k=m+1}^{n} U(a_k; b_k; t) \sum_{\ell=1}^{k-1} \beta(a_\ell - a_k)$$

Kinetic equations: solutions

Formally $\rho_n(t - \mathbf{b}_n; t)$ along characteristics starting from initial time t_0:

$$\begin{aligned}\rho_n(\mathbf{a}_n;t) =& U_n(\mathbf{a}_n;t_0;t)\rho_n(\mathbf{a}_n-(t-t_0);t_0)\\ &+(n+1)\int_{t_0}^{t} U_n(\mathbf{a}_n;t';t)\left[\int_0^{\infty}\mu_{n+1}(y)\rho_{n+1}(\mathbf{a}_n-(t-t'),y;t')\mathrm{d}y\right]\mathrm{d}t',\end{aligned}$$

in which

$$\begin{aligned}U_n(\mathbf{a}_m;t';t) &= \exp\left[-\sum_{i=1}^{m}\int_{t'}^{t}\gamma_n(a_i-(t-s))\mathrm{d}s\right]\\ &\equiv U_n^{-1}(\mathbf{a}_m;t_0;t')U_n(\mathbf{a}_m;t_0;t)\end{aligned}$$

is the propagator for any set of $m \leq n$ individuals from time t' to t.

Recursion can be “solved” and simplified in certain limits...