

1 **SUPPLEMENTARY MATERIALS: ANALYSIS AND CALIBRATION**
2 **OF A LINEAR MODEL FOR STRUCTURED CELL POPULATIONS**
3 **WITH UNIDIRECTIONAL MOTION : APPLICATION TO THE**
4 **MORPHOGENESIS OF OVARIAN FOLLICLES***

5 FRÉDÉRIQUE CLÉMENT †, FRÉDÉRIQUE ROBIN ‡, AND ROMAIN YVINEC §

6 **SM1. Supplemental proofs.**

7 **SM1.1. Deterministic model.**

8 *Proof of corollary 2.10.* According to hypothesis 2.9,

9 (SM1) $\exists A > 0, \epsilon > 0$ such that $\forall a \geq A, b_j(a) + \lambda_j > \epsilon$.

10 Let $k \in \mathbb{N}$. Using hypothesis 2.2, for all $t \geq A$, we have:

11
$$0 \leq t^k b_j(t) e^{-\int_0^t [b_j(s) + \lambda_j] ds} \leq \bar{b}_j t^k e^{-\int_0^A [b_j(s) + \lambda_j] ds} e^{-\int_A^t [b_j(s) + \lambda_j] ds}.$$

12 Then, using (SM1) we obtain:

13
$$0 \leq t^k b_j(t) e^{-\int_0^t [b_j(s) + \lambda_j] ds} \leq t^k K_{A,\epsilon} e^{-\epsilon t},$$

14 where $K_{A,\epsilon}$ is a constant given by $K_{A,\epsilon} := \bar{b}_j e^{-\int_0^A [b_j(s) + \lambda_j - \epsilon] ds}$. As $\epsilon > 0$, the
15 function $t \mapsto t^k e^{-\epsilon t}$ is integrable on \mathbb{R}_+ , and we deduce that $\int_A^{+\infty} t^k e^{-\lambda_j t} d\mathcal{B}_j(t) dt <$
16 ∞ . Using the continuity of b_j (hypothesis 2.2), we conclude that $t \mapsto e^{-\lambda_j t} d\mathcal{B}_j(t) dt$
17 is integrable on \mathbb{R}_+ . \square

18 *Proof of corollary 3.1.* According to (16), we obtain:

19 (SM2) $\forall j \in \llbracket 1, \lambda_c \rrbracket, \frac{\phi^{(j)}(a)}{2[p_S^{(j)} \phi^{(j)}(0) + p_L^{(j)} \phi^{(j+1)}(0)]} = \int_a^{+\infty} b_j(s) e^{-\int_a^s \lambda_c + b_j(u) du} ds.$

20 According to remark 2.5 and hypothesis 2.7, we deduce that $\lambda_c > -\bar{b}_j, \forall j \in \llbracket 1, J \rrbracket$.

21 Hence, using also hypothesis 2.2, we have:

22
$$\frac{\phi^{(j)}(a)}{2[p_S^{(j)} \phi^{(j)}(0) + p_L^{(j)} \phi^{(j+1)}(0)]} \geq \underline{b}_j \int_a^{+\infty} e^{-(\lambda_c + \bar{b}_j)(s-a)} ds = \frac{\underline{b}_j}{\lambda_c + \bar{b}_j},$$

23 and reminding that $\lambda_c > 0$ (see remark 2.5), we also obtain the right-side of (17):

24
$$\frac{\phi^{(j)}(a)}{2[p_S^{(j)} \phi^{(j)}(0) + p_L^{(j)} \phi^{(j+1)}(0)]} \leq \int_a^{+\infty} b_j(s) e^{-\int_a^s b_j(u) du} ds$$

25
$$= [-e^{-\int_a^s b_j(u) du}]_a^{+\infty} = 1. \quad \square$$

*Submitted to the editors DATE.

†Project team MYCENAE, Centre INRIA de Paris, France. (frederique.clement@inria.fr).

‡Project team MYCENAE, Centre INRIA de Paris, France. (frederique.robin@inria.fr).

§PRC, INRA, CNRS, IFCE, Université de Tours, 37380 Nouzilly, France. (romain.yvinec@inra.fr).

SM1

27 *Proof of lemma 3.2.* For $j \in \llbracket 1, J \rrbracket$, any solution of (4) in $\mathbf{L}^1(\mathbb{R}_+)$ is given by:

$$28 \quad \hat{\phi}^{(j)}(a) = \hat{\phi}^{(j)}(0) e^{\int_0^a [\lambda_j + b_j(s)] ds} \left[1 - 2p_S^{(j)} \int_0^a b_j(s) e^{-\int_0^s [\lambda_j + b_j(u)] du} ds \right].$$

29 According to hypothesis 2.4, $1 = 2p_S^{(j)} \int_0^{+\infty} b_j(s) e^{-\int_0^s [\lambda_j + b_j(u)] du} ds$, thus

$$30 \quad \hat{\phi}^{(j)}(a) = 2p_S^{(j)} \hat{\phi}^{(j)}(0) \int_a^{+\infty} b_j(s) e^{-\int_a^s [\lambda_j + b_j(u)] du} ds.$$

31 Finally, according to remark 2.5, $\lambda_j > -\bar{b}_j$ and we obtain, using hypothesis 2.2,

$$32 \quad \frac{\hat{\phi}^{(j)}(a)}{\hat{\phi}^{(j)}(0)} = 2p_S^{(j)} \int_a^{+\infty} b_j(s) e^{-\int_a^s [\lambda_j + b_j(u)] du} ds$$

$$33 \quad \geq 2p_S^{(j)} \underline{b}_j \int_a^{+\infty} e^{-(\lambda_j + \bar{b}_j)(s-a)} ds = 2p_S^{(j)} \frac{\underline{b}_j}{\lambda_j + \bar{b}_j}.$$

34 Then, we want to show that $\hat{\phi}^{(j)}(a) < \infty$ for all $a \in \mathbb{R}_+ \cup \{\infty\}$. Let

$$35 \quad I(a) := \int_a^{+\infty} b_j(s) e^{-\int_0^s [\lambda_j + b_j(u)] du} ds.$$

36 Applying an integration by part to $I(a)$, we obtain that, for all $a \geq 0$,

$$37 \quad I(a) = \left[e^{-\int_0^s [\lambda_j + b_j(u)] du} \right]_a^\infty - \lambda_j \int_a^\infty e^{-\int_0^s [\lambda_j + b_j(u)] du} ds.$$

38 Hypotheses 2.4 and 2.2 imply that, for all $a \geq 0$, $\int_a^\infty e^{-\int_0^s [\lambda_j + b_j(u)] du} ds < \infty$ and so,

39 $\lim_{s \rightarrow 0} e^{-\int_0^s [\lambda_j + b_j(u)] du} = 0$. Thus, we have:

$$40 \quad (\text{SM3}) \quad I(a) = e^{-\int_0^a [\lambda_j + b_j(u)] du} - \lambda_j \int_a^\infty e^{-\int_0^s [\lambda_j + b_j(u)] du} ds.$$

41 Multiplying (SM3) by $e^{\int_0^a [\lambda_j + b_j(u)] du}$, we deduce:

$$42 \quad (\text{SM4}) \quad \frac{\hat{\phi}^{(j)}(a)}{2p_S^{(j)} \hat{\phi}^{(j)}(0)} = 1 - \lambda_j \int_a^\infty e^{-\int_a^s [\lambda_j + b_j(u)] du} ds.$$

43 If $\lambda_j \geq 0$, we deduce directly from (SM4) that, for all $a \in \mathbb{R}_+ \cup \{\infty\}$, $\frac{\hat{\phi}^{(j)}(a)}{2p_S^{(j)} \hat{\phi}^{(j)}(0)} \leq 1$.

44 We assume that $\lambda_j < 0$. Using hypothesis 2.9, we deduce that there exists constants

45 $A > 0$ and $\epsilon > 0$ such that

$$46 \quad \forall a \geq A, \quad \lambda_j + b_j(a) > \epsilon > 0.$$

47 Hence, with $C = \frac{-\lambda_j}{\epsilon} > 0$, we have:

$$48 \quad \forall a \geq A, \quad -\lambda_j \leq C(\lambda_j + b_j(a)).$$

49 Applying this inequality to (SM4), we obtain:

$$50 \quad \forall a \geq A, \quad \frac{\hat{\phi}^{(j)}(a)}{2p_S^{(j)} \hat{\phi}^{(j)}(0)} \leq 1 + C \int_a^\infty [\lambda_j + b_j(s)] e^{-\int_0^s [\lambda_j + b_j(u)] du} ds \times e^{\int_0^a [\lambda_j + b_j(s)] ds}.$$

53 Again, using hypotheses 2.4 and 2.2, we obtain:

$$54 \quad \int_a^\infty [\lambda_j + b_j(s)] e^{-\int_0^s [\lambda_j + b_j(u)] du} ds = \left[-e^{-\int_0^s [\lambda_j + b_j(u)] du} \right]_a^\infty = e^{-\int_0^a [\lambda_j + b_j(u)] du}.$$

55 We deduce

$$56 \quad \forall a \geq A, \quad \frac{\hat{\phi}^{(j)}(a)}{2p_S^{(j)} \hat{\phi}^{(j)}(0)} \leq 1 + C.$$

57 As $\hat{\phi}^{(j)}$ is continuous, we conclude that

$$58 \quad \forall a \in \mathbb{R}_+ \cup \{+\infty\}, \quad \frac{\hat{\phi}^{(j)}(a)}{2p_S^{(j)} \hat{\phi}^{(j)}(0)} < \infty.$$

59

□

60 *Proof of lemma 3.3.* Deriving $\ll e^{-\lambda_c t} \rho(t, \cdot), \phi \gg$ with respect to t , we obtain

$$61 \quad \frac{d}{dt} \ll e^{-\lambda_c t} \rho(t, \cdot), \phi \gg = -e^{-\lambda_c t} \ll (\lambda_c \mathbf{1} + \mathcal{B} + \partial_a) \rho(t, \cdot), \phi \gg.$$

62 By integration by part and using that $\rho \in \mathbf{L}^1(\mathbb{R}_+)^J$ and $\phi \in \mathcal{C}_b^1(\mathbb{R}_+)^J$, we have

$$63 \quad \ll \partial_a \rho(t, \cdot), \phi \gg = -\rho(t, 0)^T \phi(0) - \ll \rho(t, \cdot), \partial_a \phi \gg,$$

64 and we deduce

65

$$66 \quad \frac{d}{dt} \ll e^{-\lambda_c t} \rho(t, \cdot), \phi \gg = e^{-\lambda_c t} [\rho(t, 0)^T \phi(0) + \ll \rho(t, \cdot), \partial_a \phi \gg \\ 67 \quad - \ll (\lambda_c \mathbf{1} + \mathcal{B}) \rho(t, \cdot), \phi \gg].$$

69 As we have $(\lambda_c \mathbf{1} + \mathcal{B})^T = (\lambda_c \mathbf{1} + \mathcal{B})$, it comes $\ll \rho(t, \cdot), \partial_a \phi \gg = \ll (\lambda_c \mathbf{1} + \mathcal{B}) \rho(t, \cdot), \phi \gg$
 70 $= \ll \rho(t, \cdot), \partial_a \phi - (\lambda_c \mathbf{1} + \mathcal{B}) \phi \gg$. Then, using that $\mathcal{L}^D \phi = \lambda_c \phi$, we deduce $(\partial_a - \lambda_c \mathbf{1} -$
 71 $\mathcal{B}) \phi = -K(\cdot)^T \phi(0)$. Thus,

$$72 \quad \frac{d}{dt} \ll e^{-\lambda_c t} \rho(t, \cdot), \phi \gg = e^{-\lambda_c t} [\rho(t, 0)^T \phi(0) - \ll \rho(t, \cdot), K(\cdot)^T \phi(0) \gg].$$

Note that $\ll \rho(t, \cdot), K(\cdot)^T \phi(0) \gg = \ll K(\cdot) \rho(t, \cdot), \phi(0) \gg = \rho(t, 0)^T \phi(0)$. Consequently,

$$\frac{d}{dt} \ll e^{-\lambda_c t} \rho(t, \cdot), \phi \gg = 0.$$

73 Hence,

$$74 \quad \forall t, \quad \ll e^{-\lambda_c t} \rho(t, \cdot), \phi \gg = \ll \rho_0(\cdot), \phi \gg = \eta.$$

75 Thanks to the renormalization $\ll \hat{\rho}, \phi \gg = 1$, we obtain the conservation principle:

$$76 \quad \ll e^{-\lambda_c t} \rho(t, \cdot) - \eta \hat{\rho}, \phi \gg = \ll e^{-\lambda_c t} \rho(t, \cdot), \phi \gg - \eta \ll \hat{\rho}, \phi \gg = 0.$$

77

□

78 *Proof of lemma 3.4.* From the linearity of the system, it can be easily shown that
 79 h is solution of

$$80 \quad \begin{cases} \partial_t h(t, a) + \partial_a h(t, a) + [\lambda_c + B(a)]h(t, a) = 0, & t \geq 0, \quad a \geq 0, \\ h(t, a = 0) = \int_0^\infty K(a)h(t, a)da. \end{cases}$$

81 Let f be a derivable function. Applying the chain rules, it comes, for $j \in \llbracket 1, J \rrbracket$,

$$82 \quad \begin{aligned} \partial_t f[h^{(j)}(t, a)] + \partial_a f[h^{(j)}(t, a)] &= f'(h^{(j)}(t, a))[\partial_t h^{(j)}(t, a) + \partial_a h^{(j)}(t, a)] \\ &= -[\lambda_c + b_j(a)] \times h^{(j)}(t, a) f'(h^{(j)}(t, a)). \end{aligned}$$

83 For $f(x) = |x|$, $f'(x) = \frac{|x|}{x}$, we deduce

$$84 \quad \partial_t |h^{(j)}(t, a)| + \partial_a |h^{(j)}(t, a)| = -[\lambda_c + b_j(a)] |h^{(j)}(t, a)|.$$

85 □

86 **LEMMA SM1.1.** [*Modified Grönwall lemma*] Let $N \in \mathbb{N}^*$. Suppose that $\forall i \in$
 87 $\llbracket 1, N \rrbracket$, there exist $\kappa_i \in \mathbb{R}_+^*$, $\gamma \in \mathbb{R}_+^*$ and P_i polynomials of degree $\alpha_i \in \mathbb{N}$ such
 88 that

$$89 \quad F'(t) \leq \sum_{i=1}^N P_i(t) e^{-\kappa_i t} - \gamma F(t).$$

90 Then,

$$91 \quad F(t) \leq K e^{-\gamma t} + \sum_{i=1}^N \tilde{P}_i(t) e^{-\kappa_i t},$$

92 where K is a constant and for all $i \in \llbracket 1, N \rrbracket$, \tilde{P}_i is a polynomial of degree $\tilde{\alpha}_i \leq \alpha_i + 1$.

93 *Proof.* Note that $\frac{d}{dt}(e^{\gamma t} F(t)) = (F'(t) + \gamma F(t)) \times e^{\gamma t}$. Hence,

$$94 \quad \frac{d}{dt}(e^{\gamma t} F(t)) \leq \sum_{i=1}^N P_i(t) e^{(-\kappa_i + \gamma)t}.$$

95 Then, integrating on the interval $[0, t]$, we obtain:

$$96 \quad e^{\gamma t} F(t) - F(0) \leq \sum_{i=1}^N \tilde{P}_i(t) e^{(\gamma - \kappa_i)t} + K$$

$$97 \quad F(t) \leq (F(0) + K) e^{-\gamma t} + \sum_{i=1}^N \tilde{P}_i(t) e^{-\kappa_i t},$$

99 where K is a constant and for all $i \in \llbracket 1, N \rrbracket$, \tilde{P}_i a polynomial of degree $\tilde{\alpha}_i \leq \alpha_i + 1$
 100 (the degree increases when $\gamma = \kappa_i$). □

101 **SM1.2. Stochastic model.** For any $f : (t, a) \mapsto (f_t^{(j)}(a))_{j \in \llbracket 1, J \rrbracket} \in \mathcal{B}_b^1(\mathbb{R}_+ \times$
 102 $\mathbb{R}_+, \mathbb{R})^J$ (the space product of the set of bounded functions with bounded derivatives),
 103 we note ∂_1 and ∂_2 respectively its derivative with respect to time (t) and age (a).

104 LEMMA SM1.2. Let $F \in \mathcal{C}^1(\mathbb{R}, \mathbb{R})$, $f \in \mathcal{B}_b^1(\mathbb{R}_+ \times \mathbb{R}_+, \mathbb{R})^J$.

$$\begin{aligned}
 F[\ll Z_t, f_t \gg] &= F[\ll f_0, Z_0 \gg] + \int_0^t \ll \partial_1 f_s + \partial_2 f_s, Z_s \gg F'[\ll f_s, Z_s \gg] ds \\
 &\quad + \int_{[0,t] \times \mathcal{E}} \left[\mathbf{1}_{k \leq N_{s^-}} \left(F[\ll f_s, 2\delta_{I_{s^-}^{(k)}, 0} - \delta_{I_{s^-}^{(k)}, A_{s^-}^{(k)} + Z_{s^-} \gg}] \right. \right. \\
 &\quad \quad \left. \left. - F[\ll f_s, Z_{s^-} \gg] \right) \mathbf{1}_{0 \leq \theta \leq m_1(s,k,Z)} \right. \\
 105 &\quad \left. + \left(F[\ll f_s, \delta_{I_{s^-}^{(k)}+1, 0} + \delta_{I_{s^-}^{(k)}, 0} - \delta_{I_{s^-}^{(k)}, A_{s^-}^{(k)} + Z_{s^-} \gg}] \right. \right. \\
 &\quad \quad \left. \left. - F[\ll f_s, Z_{s^-} \gg] \right) \mathbf{1}_{m_1(s,k,Z) \leq \theta \leq m_2(s,k,Z)} \right. \\
 &\quad \left. + \left(F[\ll f_s, 2\delta_{I_{s^-}^{(k)}+1, 0} - \delta_{I_{s^-}^{(k)}, A_{s^-}^{(k)} + Z_{s^-} \gg}] \right. \right. \\
 &\quad \quad \left. \left. - F[\ll f_s, Z_{s^-} \gg] \right) \mathbf{1}_{m_2(s,k,Z) \leq \theta \leq m_3(s,k,Z)} \right] Q(ds, dk, d\theta).
 \end{aligned}$$

106 *Proof.* We integrate f_t against the measure Z_t

$$\begin{aligned}
 \ll Z_t, f_t \gg &= \sum_{k=1}^{N_0} f_t^{(I_0^{(k)})}(A_0^{(k)} + t) \\
 &+ \int_{[0,t] \times \mathcal{E}} \left[\mathbf{1}_{k \leq N_{s^-}} \left(2f_t^{(I_{s^-}^{(k)})}(t-s) - f_t^{(I_{s^-}^{(k)})}(A_{s^-}^{(k)} + t-s) \right) \mathbf{1}_{0 \leq \theta \leq m_1(s,k,Z)} \right. \\
 107 &+ \left(f_t^{(I_{s^-}^{(k)})}(t-s) + f_t^{(I_{s^-}^{(k)}+1)}(t-s) - f_t^{(I_{s^-}^{(k)})}(A_{s^-}^{(k)} + t-s) \right) \mathbf{1}_{m_1(s,k,Z) \leq \theta \leq m_2(s,k,Z)} \\
 &+ \left. \left(2f_t^{(I_{s^-}^{(k)}+1)}(t-s) - f_t^{(I_{s^-}^{(k)})}(A_{s^-}^{(k)} + t-s) \right) \mathbf{1}_{m_2(s,k,Z) \leq \theta \leq m_3(s,k,Z)} \right] Q(ds, dk, d\theta).
 \end{aligned}$$

108 Derivating $f_t^{(j)}[a+t-s]$, we obtain

$$\begin{aligned}
 &\frac{d}{dt} \left[f_t^{(j)}[a+t-s] \right] = \partial_1 f_t^{(j)}[a+t-s] + \partial_2 f_t^{(j)}[a+t-s] \\
 109 &\Rightarrow \int_s^t \frac{d}{du} \left[f_u^{(j)}[a+u-s] \right] du = \int_s^t \left[\partial_1 f_u^{(j)}[a+u-s] + \partial_2 f_u^{(j)}[a+u-s] \right] du \\
 &\Rightarrow f_t^{(j)}[a+t-s] = f_s^{(j)}[a] + \int_s^t \left[\partial_1 f_u^{(j)}[a+u-s] + \partial_2 f_u^{(j)}[a+u-s] \right] du.
 \end{aligned}$$

110 Then, replacing j by the index $I_{s^-}^{(k)}$ and a by $A_{s^-}^{(k)}$ or 0, it comes

$$\begin{aligned}
 \ll Z_t, f_t \gg &= \sum_{k=1}^{N_0} f_0^{(I_0^{(k)})}(A_0^{(k)}) + T_0 + T_1 + T_2 + T_3 \\
 &+ \int_{[0,t] \times \mathcal{E}} \mathbf{1}_{k \leq N_{s^-}} \left[\left(2f_s^{(I_{s^-}^{(k)})}(0) - f_s^{(I_{s^-}^{(k)})}(A_{s^-}^{(k)}) \right) \mathbf{1}_{0 \leq \theta \leq m_1(s,k,Z)} \right. \\
 111 &+ \left(f_s^{(I_{s^-}^{(k)})}(0) + f_s^{(I_{s^-}^{(k)}+1)}(0) - f_s^{(I_{s^-}^{(k)})}(A_{s^-}^{(k)}) \right) \mathbf{1}_{m_1(s,k,Z) \leq \theta \leq m_2(s,k,Z)} \\
 &+ \left. \left(2f_s^{(I_{s^-}^{(k)}+1)}(0) - f_s^{(I_{s^-}^{(k)})}(A_{s^-}^{(k)}) \right) \mathbf{1}_{m_2(s,k,Z) \leq \theta \leq m_3(s,k,Z)} \right] Q(ds, dk, d\theta),
 \end{aligned}$$

112 where

$$T_0 = \sum_{k=1}^{N_0} \int_0^t \left[\partial_1 f_u^{(I_0^{(k)})} (A_0^{(k)} + u) + \partial_2 f_u^{(I_0^{(k)})} (A_0^{(k)} + u) \right] du,$$

$$T_1 = \int_{[0,t] \times \mathcal{E}} \mathbb{1}_{k \leq N_{s^-}} \int_s^t \left[2\partial_1 f_u^{(I_{s^-}^{(k)})} (u-s) \right. \\ \left. + 2\partial_2 f_u^{(I_{s^-}^{(k)})} (u-s) - \partial_1 f_u^{(I_{s^-}^{(k)})} (A_{s^-}^{(k)} + u-s) \right. \\ \left. - \partial_2 f_u^{(I_{s^-}^{(k)})} (A_{s^-}^{(k)} + u-s) \mathbb{1}_{0 \leq \theta \leq m_1(s,k,Z)} \right] du Q(ds, dk, d\theta),$$

113

$$T_2 = \int_{[0,t] \times \mathcal{E}} \mathbb{1}_{k \leq N_{s^-}} \int_s^t \left[\partial_1 f_u^{(I_{s^-}^{(k)})} (u-s) + \partial_1 f_u^{(I_{s^-}^{(k)+1})} (u-s) + \partial_2 f_u^{(I_{s^-}^{(k)})} (u-s) \right. \\ \left. + \partial_2 f_u^{(I_{s^-}^{(k)+1})} (u-s) - \partial_1 f_u^{(I_{s^-}^{(k)})} (A_{s^-}^{(k)} + u-s) \right. \\ \left. - \partial_2 f_u^{(I_{s^-}^{(k)})} (A_{s^-}^{(k)} + u-s) \mathbb{1}_{m_1(s,k,Z) \leq \theta \leq m_2(s,k,Z)} \right] du Q(ds, dk, d\theta),$$

$$T_3 = \int_{[0,t] \times \mathcal{E}} \mathbb{1}_{k \leq N_{s^-}} \int_s^t \left[2\partial_1 f_u^{(I_{s^-}^{(k)+1})} (u-s) \right. \\ \left. + 2\partial_2 f_u^{(I_{s^-}^{(k)+1})} (u-s) - \partial_1 f_u^{(I_{s^-}^{(k)})} (A_{s^-}^{(k)} + u-s) \right. \\ \left. - \partial_2 f_u^{(I_{s^-}^{(k)})} (A_{s^-}^{(k)} + u-s) \mathbb{1}_{m_2(s,k,Z) \leq \theta \leq m_3(s,k,Z)} \right] du Q(ds, dk, d\theta).$$

114 As the partial differential of each $f^{(j)}$ are uniformly bounded, we can apply Fubini
115 theorem on T_0 , T_1 , T_2 and T_3 :

$$T_0 = \int_0^t \ll \partial_1 f_u + \partial_2 f_u, \sum_{k=1}^{N_0} \delta_{I_0^{(k)}, A_0^{(k)} + u} \gg du,$$

$$T_1 = \int_0^t \left[\ll \partial_1 f_u + \partial_2 f_u, \int_0^u \int_{\mathcal{E}} \mathbb{1}_{k \leq N_{s^-}} \left(2\delta_{I_{s^-}^{(k)}, u-s} \right. \right. \\ \left. \left. - \delta_{I_{s^-}^{(k)}, A_{s^-}^{(k)} + u-s} \right) \mathbb{1}_{0 \leq \theta \leq m_1(s,k,Z)} Q(ds, dk, d\theta) \gg \right] du,$$

116

$$T_2 = \int_0^t \left[\ll \partial_1 f_u + \partial_2 f_u, \int_0^u \int_{\mathcal{E}} \mathbb{1}_{k \leq N_{s^-}} \left(\delta_{I_{s^-}^{(k)}, u-s} + \delta_{I_{s^-}^{(k)+1}, u-s} \right. \right. \\ \left. \left. - \delta_{I_{s^-}^{(k)}, A_{s^-}^{(k)} + u-s} \right) \mathbb{1}_{m_1(s,k,Z) \leq \theta \leq m_2(s,k,Z)} Q(ds, dk, d\theta) \gg \right] du,$$

$$T_3 = \int_0^t \left[\ll \partial_1 f_u + \partial_2 f_u, \int_0^u \int_{\mathcal{E}} \mathbb{1}_{k \leq N_{s^-}} \left(2\delta_{I_{s^-}^{(k)+1}, u-s} \right. \right. \\ \left. \left. - \delta_{I_{s^-}^{(k)}, A_{s^-}^{(k)} + u-s} \right) \mathbb{1}_{m_2(s,k,Z) \leq \theta \leq m_3(s,k,Z)} Q(ds, dk, d\theta) \gg \right] du.$$

117 Finally, using the stochastic differential equation (2)

$$118 \quad T_0 + T_1 + T_2 + T_3 = \int_0^t \ll f_u + \partial_2 f_u, Z_u \gg du.$$

119 Consequently, we obtain

$$\begin{aligned} & \ll f_t, Z_t \gg = \ll f_0, Z_0 \gg + \int_0^t \ll \partial_1 f_s + \partial_2 f_s, Z_s \gg ds \\ & + \int_{[0,t] \times \mathcal{E}} \mathbb{1}_{k \leq N_{s-}} \left[\ll f_s, 2\delta_{I_{s-}^{(k)}, 0} - \delta_{I_{s-}^{(k)}, A_{s-}^{(k)}} \gg \mathbb{1}_{0 \leq \theta \leq m_1(s,k,Z)} \right. \\ & + \ll f_s, \delta_{I_{s-}^{(k)}, 0} + \delta_{I_{s-}^{(k)+1, 0} - \delta_{I_{s-}^{(k)}, A_{s-}^{(k)}} \gg \mathbb{1}_{m_1(s,k,Z) \leq \theta \leq m_2(s,k,Z)} \\ & \left. + \ll f_s, 2\delta_{I_{s-}^{(k)+1, 0} - \delta_{I_{s-}^{(k)}, A_{s-}^{(k)}} \gg \mathbb{1}_{m_2(s,k,Z) \leq \theta \leq m_3(s,k,Z)} \right] Q(ds, dk, d\theta), \end{aligned}$$

121 which gives us lemma SM1.2 for $F(x) = x$. We conclude by applying the Ito's formula
122 (see [SM5], p.68-70). \square

123 We introduce the sequence of stopping times ξ_N .

124 DEFINITION SM1.3. Let ξ_N a sequence of stopping times defined as

$$125 \quad \xi_N = \sup \{ t : N_t < N, \ll a, Z_t \gg < N \}.$$

126 *Proof of theorem 3.6.* We first start by showing (32).

$$127 \quad N_t = N_0 + \int_{[0,t] \times \mathcal{E}} \mathbb{1}_{k \leq N_{s-}} \mathbb{1}_{0 \leq \theta \leq b_{I_{s-}^{(k)}}(A_{s-}^{(k)})} Q(ds, dk, d\theta).$$

128 Thus,

$$129 \quad \sup_{s \leq t \wedge \xi_N} N_s \leq N_0 + \int_0^{t \wedge \xi_N} \int_{\mathcal{E}} \mathbb{1}_{k \leq N_{s-}} \mathbb{1}_{0 \leq \theta \leq \bar{b}} Q(ds, dk, d\theta),$$

130 where $\bar{b} := \sup_{j \in [0, J]} \bar{b}_j$. Taking the expectation and using Poisson measure properties,

131 we obtain

$$132 \quad \mathbb{E} \left[\sup_{s \leq t \wedge \xi_N} N_s \right] \leq \mathbb{E}[N_0] + \bar{b} \mathbb{E} \left[\int_0^{t \wedge \xi_N} N_s ds \right] \leq \mathbb{E}[N_0] + \bar{b} \mathbb{E} \left[\int_0^{t \wedge \xi_N} \sup_{u \leq s \wedge \xi_N} N_u ds \right].$$

133 Hence,

$$134 \quad \mathbb{E} \left[\sup_{s \leq t \wedge \xi_N} N_s \right] \leq \mathbb{E}[N_0] + \bar{b} \mathbb{E} \left[\int_0^t \sup_{u \leq s \wedge \xi_N} N_u ds \right].$$

135 By Fubini theorem, we deduce that

$$136 \quad \mathbb{E} \left[\sup_{s \leq t \wedge \xi_N} N_s \right] \leq \mathbb{E}[N_0] + \bar{b} \int_0^t \mathbb{E} \left[\sup_{u \leq s \wedge \xi_N} N_u \right] ds.$$

137 Applying Grönwall lemma, we deduce for all $t \leq T$ that

$$138 \quad \mathbb{E} \left[\sup_{s \leq t \wedge \xi_N} N_s \right] \leq \mathbb{E}[N_0] e^{\bar{b}t}.$$

139 Hence,

$$140 \quad \mathbb{E} \left[\sup_{t \leq T \wedge \xi_N} N_t \right] \leq \mathbb{E}[N_0] e^{\bar{b}T} < \infty.$$

141 Using the same method, we also deduce that $\mathbb{E}[\sup_{t \leq T} \ll a, Z_t \gg] < \infty$.

142 Then, we use the same approach as [SM8] (Theorem 2.2.8) to compute the in-
 143 finitesimal generator of Z_t , denoted by \mathcal{G} . By construction, $(Z_t)_{t \in \mathbb{R}_+}$ is a marko-
 144 vian process of $\mathbb{D}([0, T], \mathcal{M}_P(\llbracket 1, J \rrbracket \times \mathbb{R}_+))$. Let $f \in \mathbf{C}_b^1(\mathcal{E}, \mathbb{R})$, by definition, $\mathcal{G}F :=$
 145 $\lim_{t \rightarrow 0} \frac{d}{dt} \mathbb{E}[F[\ll f, Z_t \gg]]$. Taking the expectation of the expression of $\ll f, Z_{t \wedge \xi_N} \gg$
 146 given in lemma SM1.2, we obtain

$$147 \quad \mathbb{E}[F[\ll f, Z_{t \wedge \xi_N} \gg]] = \mathbb{E}[F[\ll f, Z_0 \gg]] \\ + \mathbb{E} \left[\int_0^{t \wedge \xi_N} \ll \partial_a f, Z_s \gg F'[\ll f, Z_s \gg] ds \right] + \mathbb{E}[\chi^{f,F}(t \wedge \xi_N, Z)],$$

148 where

$$\begin{aligned} \chi^{f,F}(t, Z) := & \int_0^t \int_{\mathcal{E}} \left[(F[\ll f, 2\delta_{j,0} - \delta_{j,a} + Z_s \gg] - F[\ll f, Z_s \gg]) p_{2,0}^{(j)} \right. \\ & + (F[\ll f, \delta_{j+1,0} + \delta_{j,0} - \delta_{j,a} + Z_s \gg] - F[\ll f, Z_s \gg]) p_{1,1}^{(j)} \\ & + (F[\ll f, 2\delta_{j+1,0} - \delta_{j,a} + Z_s \gg] \\ & \left. - F[\ll f, Z_s \gg]) p_{0,2}^{(j)} \right] b_j(a) Z_s(dj, da) ds. \end{aligned}$$

150 We have the following estimates,

$$151 \quad \mathbb{E}[\chi^{f,F}(t \wedge \xi_N, Z)] \leq 2\mathbb{E}[\sup_{t \leq T} N_t] T \|F\|_{\infty} \bar{b},$$

$$\mathbb{E}[\int_0^{t \wedge \xi_N} \ll \partial_a f, Z_s \gg F'[\ll f, Z_s \gg] ds] \leq \mathbb{E}[\sup_{t \leq T} N_t] T \times \|\partial_a f\|_{\infty} \times \|F'\|_{\infty}.$$

Those bounds are independent of N thanks to (32), so that we may let N goes to infinity. Moreover,

$$\frac{d}{dt} \int_0^t \ll \partial_a f, Z_s \gg F'[\ll f, Z_s \gg] ds = \ll \partial_a f, Z_t \gg F'[\ll f, Z_t \gg]$$

152 which is also dominated by $\mathbb{E}[\sup_{t \leq T} N_t] \times \|\partial_a f\|_{\infty} \times \|F'\|_{\infty}$. Also,

$$\begin{aligned} \frac{\partial}{\partial t} \chi(t, Z_t) = & \int_{\mathcal{E}} \left[(F[\ll f, 2\delta_{j,0} - \delta_{j,a} + Z_t \gg] - F[\ll f, Z_t \gg]) p_{2,0}^{(j)} \right. \\ & + (F[\ll f, \delta_{j+1,0} + \delta_{j,0} - \delta_{j,a} + Z_t \gg] - F[\ll f, Z_t \gg]) p_{1,1}^{(j)} \\ & \left. + (F[\ll f, 2\delta_{j+1,0} - \delta_{j,a} + Z_t \gg] - F[\ll f, Z_t \gg]) p_{0,2}^{(j)} \right] b_j(a) Z_t(dj, da). \end{aligned}$$

154 $|\frac{\partial}{\partial t} \chi(t, Z_t)|$ is dominated \mathbb{P} -p.s by $2\mathbb{E}[\sup_{t \leq T} N_t] \|F\|_{\infty} \bar{b}$. We can thus apply the
 155 differentiating theorem under the integral sign \mathbb{E} and conclude. \square

156 *Proof of lemma 3.7.* Introducing the compensated Poisson measure \tilde{Q} ,
 157 $\tilde{Q}(ds, dk, d\theta) := Q(ds, dk, d\theta) - dsdkd\theta$, we define the process:

$$\begin{aligned}
 M_t^{F,f} := & \int \int_{[0,t] \wedge \xi_N \times \mathcal{E}} \mathbf{1}_{k < N_{s-}} \left[\left(F[\ll f, 2\delta_{I_{s-}^k, 0} - \delta_{I_{s-}^k, A_{s-}^k} + Z_{s-} \gg] \right. \right. \\
 & \left. \left. - F[\ll f, Z_{s-} \gg] \right) \mathbf{1}_{0 \leq \theta \leq m_1(s,k,Z)} \right. \\
 & + \left(F[\ll f, \delta_{I_{s-}^k+1, 0} + \delta_{I_{s-}^k, 0} - \delta_{I_{s-}^k, A_{s-}^k} + Z_{s-} \gg] \right. \\
 158 & \left. - F[\ll f, Z_{s-} \gg] \right) \mathbf{1}_{m_1(s,k,Z) \leq \theta \leq m_2(s,k,Z)} \\
 & + \left(F[\ll f, 2\delta_{I_{s-}^k+1, 0} - \delta_{I_{s-}^k, A_{s-}^k} + Z_{s-} \gg] \right. \\
 & \left. - F[\ll f, Z_{s-} \gg] \right) \mathbf{1}_{m_2(s,k,Z) \leq \theta \leq m_3(s,k,Z)} \tilde{Q}(ds, dk, d\theta).
 \end{aligned}$$

159 We can verify that $M_t^{F,f}$ is a martingale as an integral against a compensated
 160 Poisson measure. Then, applying lemma SM1.2 and the definition of the generator
 161 given in theorem 3.6, we show that

$$162 \text{ (SM5)} \quad M_t^{F,f} = F[\ll f, Z_t \gg] - F[\ll f, Z_0 \gg] - \int_0^t \mathcal{G}F[\ll f, Z_s \gg] ds.$$

163 We turn now to the computation of the quadratic variation and use the same approach
 164 as in [SM1]. We apply (SM5) for $F(x) = x^2$. Note that we cannot use directly this
 165 result as $x \mapsto x^2$ is not bounded and we need to first use a localizing sequence (see
 166 [SM4] p. 382, theorem 13.14). We obtain that

$$\begin{aligned}
 & \ll f, Z_t \gg^2 - \ll f, Z_0 \gg^2 - \int_0^t 2 \ll f, Z_s \gg \times \ll \partial_a f, Z_s \gg ds \\
 167 \text{ (SM6)} \quad & - \int_0^t \sum_{j=1}^J \int_{\mathbb{R}_+} \left[(\ll f, 2\delta_{j,0} - \delta_{j,a} + Z_s \gg^2 - \ll f, Z_s \gg^2) b_j(a) p_{2,0}^{(j)} \right. \\
 & \left. - (\ll f, \delta_{j,0} + \delta_{j+1,0} - \delta_{j,a} + Z_s \gg^2 - \ll f, Z_s \gg^2) b_j(a) p_{1,1}^{(j)} Z_s(dj, da) \right. \\
 & \left. - (\ll f, 2\delta_{j+1,0} - \delta_{j,a} + Z_s \gg^2 - \ll f, Z_s \gg^2) b_j(a) p_{0,2}^{(j)} Z_s(dj, da) ds \right]
 \end{aligned}$$

168 is a martingale. Then, applying (SM5) for $F(x) = x$ (using a localizing sequence
 169 again), we get that

$$\begin{aligned}
 \ll f, Z_t \gg & = \ll f, Z_0 \gg + \int_0^t \ll \partial_a f, Z_s \gg ds \\
 & + \int_0^t \left[\sum_{j=1}^J \int_{\mathbb{R}_+} \ll f, 2\delta_{j,0} - \delta_{j,a} \gg b_j(a) p_{2,0}^{(j)} Z_s(dj, da) \right] ds \\
 170 & + \int_0^t \left[\sum_{j=1}^J \int_{\mathbb{R}_+} \ll f, \delta_{j,0} + \delta_{j+1,0} - \delta_{j,a} \gg b_j(a) p_{1,1}^{(j)} Z_s(dj, da) \right] ds \\
 & + \int_0^t \left[\sum_{j=1}^J \int_{\mathbb{R}_+} \ll f, 2\delta_{j+1,0} - \delta_{j,a} \gg b_j(a) p_{0,2}^{(j)} Z_s(dj, da) \right] ds + M_t^f
 \end{aligned}$$

171 is a semi-martingale. Applying the Ito formula (see [SM5], p. 78-79), we obtain:

$$\begin{aligned}
& \ll f, Z_t \gg^2 - \ll f, Z_0 \gg^2 - \int_0^t 2 \ll f, Z_s \gg \times \ll \partial_a f, Z_s \gg ds \\
& + \sum_{j=1}^J \int_{\mathbb{R}_+} (2 \ll f, Z_s \gg \times \ll f, 2\delta_{j,0} - \delta_{j,a} \gg) b_j(a) p_{2,0}^{(j)} Z_s(dj, da) \\
172 \quad (\text{SM7}) & + \sum_{j=1}^J \int_{\mathbb{R}_+} (2 \ll f, Z_s \gg \times \ll f, \delta_{j,0} + \delta_{j+1,0} - \delta_{j,a} \gg) b_j(a) p_{1,1}^{(j)} Z_s(dj, da) \\
& + \sum_{j=1}^J \int_{\mathbb{R}_+} (2 \ll f, Z_s \gg \times \ll f, 2\delta_{j+1,0} - \delta_{j,a} \gg) b_j(a) p_{0,2}^{(j)} Z_s(dj, da) ds \\
& - \langle M^f, M^f \rangle_t
\end{aligned}$$

173 is a martingale. We consider the jump corresponding to the case when the two
174 daughter cells remain on their mother layer. Note that

$$\begin{aligned}
175 \quad & \ll f, 2\delta_{j,0} - \delta_{j,a} + Z_s \gg^2 - \ll f, Z_s \gg^2 = \\
& 2 \ll f, Z_s \gg \times \ll f, 2\delta_{j,0} - \delta_{j,a} \gg + \ll f, 2\delta_{j,0} - \delta_{j,a} \gg^2.
\end{aligned}$$

176 We proceed similarly for the two other jumps. Applying the Doob-Meyer theorem
177 ([SM5], p. 106), we deduce the quadratic variation $\langle M^f, M^f \rangle_t$ comparing (SM6) and
178 (SM7). \square

179 SM1.3. Moment study.

180 *Generating functions.*

Proof of lemma 3.9. Let $a \geq 0$. Remind that the generating function is given by

$$F^{(i,a)}[\mathbf{s}; t] = \sum_{\mathbf{k} \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}} \mathbb{P}[Y_t^a = \mathbf{k} | Z_0 = \delta_{i,0}].$$

181 Let $i \in \llbracket 1, J \rrbracket$ and $\mathbf{j}, \mathbf{k} \in \mathbb{N}^J$. We note $P_{\mathbf{j}, \mathbf{k}}^a(t) := \mathbb{P}[Y_t^a = \mathbf{k} | Z_0 = \sum_{i=1}^J j_i \delta_{i,0}]$. We
182 write the backward equation for the probability $P_{e_i, \mathbf{k}}^a(t) := \mathbb{P}[Y_t^a = \mathbf{k} | Z_0 = \delta_{i,0}]$.
183 Starting from a single mother cell of age 0 and layer i , there are three possibilities at
184 time t : (i) the cell has not divided and $t \leq a$, (ii) the cell has not divided and $t > a$,
185 and (iii) the cell has divided. Thus,

$$\begin{aligned}
187 \quad (\text{SM8}) \quad & P_{e_i, \mathbf{k}}^a(t) = (\delta_{e_i, \mathbf{k}} \mathbb{1}_{t \leq a} + \delta_{\mathbf{0}, \mathbf{k}} \mathbb{1}_{t > a}) \mathbb{P}[\tau^{(i)}(a_0 = 0) \geq t] \\
& + \int_0^t [p_{2,0}^{(i)} P_{2e_i, \mathbf{k}}^a(t-y) + p_{1,1}^{(i)} P_{e_i+e_{i+1}, \mathbf{k}}^a(t-y) + p_{0,2}^{(i)} P_{2e_{i+1}, \mathbf{k}}^a(t-y)] d\mathcal{B}_i(y) dy
\end{aligned}$$

190 where $\mathbb{P}[\tau^{(i)}(a_0 = 0) \geq t] = e^{-\int_0^t b_i(s) ds} \mathbb{1}_{t \geq 0} = 1 - \mathcal{B}_i(t)$.

Applying the branching property, we have for all $y \in [0, t]$, for all $i \in \llbracket 1, J \rrbracket$

$$P_{2e_i, \mathbf{k}}^a(y) = \sum_{\mathbf{k}_1, \mathbf{k}_2 / \mathbf{k}_1 + \mathbf{k}_2 = \mathbf{k}} [P_{e_i, \mathbf{k}_1}^a(y) P_{e_i, \mathbf{k}_2}^a(y)],$$

and also, for all $i \in \llbracket 1, J-1 \rrbracket$,

$$P_{e_i+e_{i+1}, \mathbf{k}}^a(y) = \sum_{\mathbf{k}_1, \mathbf{k}_2 / \mathbf{k}_1 + \mathbf{k}_2 = \mathbf{k}} P_{e_{i+1}, \mathbf{k}_1}^a(y) P_{e_i, \mathbf{k}_2}^a(y).$$

Hence, we can rewrite the expression of

$$A_t := \int_0^t [p_{2,0}^{(i)} P_{2e_i, \mathbf{k}}^a(t-y) + p_{1,1}^{(i)} P_{e_i+e_{i+1}, \mathbf{k}}^a(t-y) + p_{0,2}^{(i)} P_{2e_{i+1}, \mathbf{k}}^a(t-y)] d\mathcal{B}_i(y) dy$$

191 as
192

$$\begin{aligned} 193 \quad A_t &= p_{2,0}^{(i)} \int_0^t \sum_{\mathbf{k}_1, \mathbf{k}_2 / \mathbf{k}_1 + \mathbf{k}_2 = \mathbf{k}} P_{e_i, \mathbf{k}_1}^a(t-y) P_{e_i, \mathbf{k}_2}^a(t-y) d\mathcal{B}_i(y) dy \\ 194 \quad &+ p_{1,1}^{(i)} \int_0^t \sum_{\mathbf{k}_1, \mathbf{k}_2 / \mathbf{k}_1 + \mathbf{k}_2 = \mathbf{k}} P_{e_{i+1}, \mathbf{k}_1}^a(t-y) P_{e_i, \mathbf{k}_2}^a(t-y) d\mathcal{B}_i(y) dy \\ 195 \quad &+ p_{0,2}^{(i)} \int_0^t \sum_{\mathbf{k}_1, \mathbf{k}_2 / \mathbf{k}_1 + \mathbf{k}_2 = \mathbf{k}} P_{e_{i+1}, \mathbf{k}_1}^a(t-y) P_{e_{i+1}, \mathbf{k}_2}^a(t-y) d\mathcal{B}_i(y) dy. \end{aligned}$$

197 Note that
198

$$\begin{aligned} 199 \quad \sum_{\mathbf{k} \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}} P_{2e_i, \mathbf{k}}^a(t-y) &= \sum_{\mathbf{k} \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}} \sum_{\mathbf{k}_1, \mathbf{k}_2 / \mathbf{k}_1 + \mathbf{k}_2 = \mathbf{k}} P_{e_i, \mathbf{k}_1}^a(t-y) P_{e_i, \mathbf{k}_2}^a(t-y) \\ 200 \quad &= \sum_{\mathbf{k} \in \mathbb{N}^J} \sum_{\mathbf{k}_1=0}^{\mathbf{k}} \mathbf{s}^{\mathbf{k}_1} P_{e_i, \mathbf{k}_1}^a(t-y) \mathbf{s}^{\mathbf{k}-\mathbf{k}_1} P_{e_i, \mathbf{k}-\mathbf{k}_1}^a(t-y). \end{aligned}$$

202 We note $\sum_{\mathbf{k}_1=0}^{\mathbf{k}}$ the sum of all the $\mathbf{k}_1 \in \mathbb{N}^J$ vectors such that $\mathbf{k}_1 \leq \mathbf{k}$ component by
203 component. We have
204

$$\begin{aligned} 205 \quad \sum_{\mathbf{k} \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}} P_{2e_i, \mathbf{k}}^a(t-y) &= \sum_{\mathbf{k} \in \mathbb{N}^J} \sum_{\mathbf{k}_1=0}^{\mathbf{k}} \mathbf{s}^{\mathbf{k}_1} P_{e_i, \mathbf{k}_1}^a(t-y) \mathbf{s}^{\mathbf{k}-\mathbf{k}_1} P_{e_i, \mathbf{k}-\mathbf{k}_1}^a(t-y) \\ 206 \quad &= \sum_{\mathbf{k}_1 \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}_1} P_{e_i, \mathbf{k}_1}^a(t-y) \sum_{\mathbf{k} \geq \mathbf{k}_1} \mathbf{s}^{\mathbf{k}-\mathbf{k}_1} P_{e_i, \mathbf{k}-\mathbf{k}_1}^a(t-y) \\ 207 \quad &= \left(\sum_{\mathbf{k}_1 \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}_1} P_{e_i, \mathbf{k}_1}^a(t-y) \right) \left(\sum_{\mathbf{k}_2 \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}_2} P_{e_i, \mathbf{k}_2}^a(t-y) \right). \end{aligned}$$

209 Hence,

$$210 \quad (\text{SM9}) \quad \sum_{\mathbf{k} \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}} P_{2e_i, \mathbf{k}}^a(t-y) = (F^{(i,a)}[\mathbf{s}; t-y])^2.$$

211 In the same way, we also obtain

$$212 \quad (\text{SM10}) \quad \sum_{\mathbf{k} \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}} P_{e_i+e_{i+1}, \mathbf{k}}^a(t-y) = F^{(i,a)}[\mathbf{s}; t-y] F^{(i+1,a)}[\mathbf{s}; t-y]$$

213 and

$$214 \quad (\text{SM11}) \quad \sum_{\mathbf{k} \in \mathbb{N}^J} \mathbf{s}^{\mathbf{k}} P_{2e_{i+1}, \mathbf{k}}^a(t-y) = (F^{(i+1,a)}[\mathbf{s}; t-y])^2.$$

215 Finally, multiplying (SM8) by $\mathbf{s}^{\mathbf{k}}$, summing on $\mathbf{k} \in \mathbb{N}^J$ and applying (SM9)-(SM11),
216 we obtain:

$$\forall i \in \llbracket 1, J \rrbracket, F^{(i,a)}[\mathbf{s}; t] = (s_i \mathbb{1}_{t \leq a} + \mathbb{1}_{t > a})(1 - \mathcal{B}_i(t)) + \int_0^t f^{(i)}(F[\mathbf{s}; t - y]) d\mathcal{B}_i(y) dy.$$

218

□

219 *First moments.*

220 *Proof of lemma 3.10.* By classical property, $M_{i,j}^a(t) = \frac{\partial}{\partial s_j} F^{(i,a)}[\mathbf{s}; t]|_{\mathbf{s}=1}$. From
 221 (38) it comes that

$$(SM12) \quad \frac{\partial}{\partial s_j} F^{(i,a)}[\mathbf{s}; t] = \delta_{i,j}(1 - \mathcal{B}_{i,i}(t)) \mathbb{1}_{a \geq t} + \int_0^t \frac{\partial}{\partial s_j} f^{(i)}[F^a(s, y)] d\mathcal{B}_i(t - y) dy$$

223 where

224

$$\begin{aligned} \frac{\partial}{\partial s_j} f^{(i)}[F^a(s, t)] &= 2p_{2,0}^{(i)} F^{(i,a)}[\mathbf{s}; t] \frac{\partial}{\partial s_j} F^{(i,a)}[\mathbf{s}; t] + 2p_{0,2}^{(i)} F^{(i+1,a)}[\mathbf{s}; t] \frac{\partial}{\partial s_j} F^{(i+1,a)}[\mathbf{s}; t] \\ &+ p_{1,1}^{(i)} [F^{(i+1,a)}[\mathbf{s}; t] \frac{\partial}{\partial s_j} F^{(i,a)}[\mathbf{s}; t] + F^{(i,a)}[\mathbf{s}; t] \frac{\partial}{\partial s_j} F^{(i+1,a)}[\mathbf{s}; t]]. \end{aligned}$$

228 For $\mathbf{s} = 1$, knowing that $F^{(i,a)}(1, t) = 1$, we get

229

$$\begin{aligned} M_{i,j}^a(t) &= \delta_{i,j}(1 - \mathcal{B}_i(t)) \mathbb{1}_{t \leq a} \\ &+ \int_0^t [2p_{2,0}^{(i)} M_{i,j}^a(y) + p_{1,1}^{(i)} [M_{i,j}^a(y) + M_{i+1,j}^a(y)] + 2p_{0,2}^{(i)} M_{i+1,j}^a(y)] d\mathcal{B}_i(t - y) dy \end{aligned}$$

233 which can be rewritten as

$$M_{i,j}^a(t) = \delta_{i,j}(1 - \mathcal{B}_i(t)) \mathbb{1}_{t \leq a} + [2p_S^{(i)} M_{i,j}^a + 2p_L^{(i)} M_{i+1,j}^a] * d\mathcal{B}_i(t).$$

235

□

236 *Harris lemmas.* We recall some results on the renewal theory presented in [SM3],
 237 p.161-163.

238 Let G be a distribution function on $(0, \infty)$ with the additional assumption $G(0+) = 0$.

239 We consider the renewal equation

$$(SM13) \quad K(t) = f(t) + m \int_0^t K(t - u) dG(u) = f(t) + mK * G(t)$$

241 where m is a positive constant representing the mean number of children, f is a
 242 continuous function representing a source term and G is the life time distribution. In
 243 addition, we suppose that G is not lattice.

244 LEMMA SM1.4 (Harris's lemma 2, p.161). *Suppose that there exists a Malthus*
 245 *parameter α such that $m \int_0^\infty e^{-\alpha t} dG(t) = 1$, and that the following conditions also*
 246 *hold:*

247 (a) $f(t)e^{-\alpha t}$ is a continuous function such that $f(t)e^{-\alpha t} \in \mathbf{L}^1(\mathbb{R}_+)$.248 (b) $\int_0^\infty t^2 dG(t) < \infty$.

249 Then, $K(t) \sim n_f e^{\alpha t}$, where

$$250 \quad n_f = \frac{\int_0^\infty f(t) e^{-\alpha t} dt}{m \int_0^\infty t e^{-\alpha t} dG(t)}.$$

251 LEMMA SM1.5 (Harris's lemma 4, p.163). Suppose that $m < 1$ and $\lim_{t \rightarrow \infty} f(t) = c$.
 252 then $K(t) \rightarrow \frac{c}{1-m}$.

253 Additional computation details for the proof of theorem 2.14. We detail how to
 254 obtain formula (49). We first take the Laplace transform of (39) for $\alpha = \lambda_c$ for
 255 $i = c + 1$ and $j \in \llbracket c + 1, J \rrbracket$. We distinguish the case $i = j$ from the others. If
 256 $j = c + 1$, we obtain

$$257 \quad \int_0^\infty M_{j,j}^a(t) e^{-\lambda_c t} dt =$$

$$258 \quad \frac{1}{\hat{\rho}^{(j)}(0)} \int_0^a \hat{\rho}^{(j)}(t) dt + 2p_S^{(j)} \int_0^\infty \left[\int_0^t d\mathcal{B}_j(t-u) M_{j,j}^a(u) du \right] e^{-\lambda_c t} dt.$$

261 By the Laplace transform property for the convolution, we deduce that

$$262 \quad \int_0^\infty \left[\int_0^t d\mathcal{B}_j(t-u) M_{j,j}^a(u) du \right] e^{-\lambda_c t} dt = d\mathcal{B}_j^*(\lambda_c) \int_0^\infty M_{j,j}^a(t) e^{-\lambda_c t} dt,$$

263 hence

$$264 \quad \int_0^\infty M_{j,j}^a(t) e^{-\lambda_c t} dt = \frac{1}{\hat{\rho}^{(j)}(0)} \int_0^a \hat{\rho}^{(j)}(t) dt + 2p_S^{(j)} d\mathcal{B}_j^*(\lambda_c) \int_0^\infty M_{j,j}^a(t) e^{-\lambda_c t} dt$$

$$265 \quad = \frac{1}{\hat{\rho}^{(j)}(0) \times (1 - 2p_S^{(j)} d\mathcal{B}_j^*(\lambda_c))} \int_0^a \hat{\rho}^{(j)}(t) dt.$$

268 When $j > c + 1$, we have:

$$269 \quad \int_0^\infty M_{c+1,j}^a(t) e^{-\lambda_c t} dt =$$

$$270 \quad 2p_S^{(c+1)} d\mathcal{B}_{c+1}^*(\lambda_c) \int_0^\infty M_{c+1,j}^a(t) e^{-\lambda_c t} dt + 2p_L^{(c+1)} d\mathcal{B}_j^*(\lambda_c) \int_0^\infty M_{c+2,j}^a(t) e^{-\lambda_c t} dt.$$

273 Hence,

$$274 \quad \int_0^\infty M_{c+1,j}^a(t) e^{-\lambda_c t} dt = \frac{2p_L^{(c+1)}}{1 - 2p_S^{(c+1)} d\mathcal{B}_{c+1}^*(\lambda_c)} \int_0^\infty M_{c+2,j}^a(t) e^{-\lambda_c t} dt.$$

275 Here, we obtain a recurrence formula between $\int_0^\infty M_{c+1,j}^a(t) e^{-\lambda_c t} dt$ and

$$276 \quad \int_0^\infty M_{c+2,j}^a(t) e^{-\lambda_c t} dt, \text{ and we obtain (49).}$$

277 Second moments.

DEFINITION SM1.6. Let $a \geq 0$. We define the second moment

$$L^a(t) := (\mathbb{E}[(Y_t^{(a,j)})^2 | Z_0 = \delta_{i,0}])_{i,j \in \llbracket 1, J \rrbracket}.$$

278 LEMMA SM1.7. $L^a(t)$ is solution of the renewal equation: $\forall(i, j) \in \llbracket 1, J \rrbracket^2$,

$$279 \quad (SM14) \quad L_{i,j}^a(t) = \delta_{i,j}(1 - \mathcal{B}_i(t))\mathbf{1}_{t \leq a} + [2p_S^{(i)}L_{i,j}^a + 2p_L^{(i)}L_{i+1,j}^a] * d\mathcal{B}_i(t) \\ + [2p_{2,0}^{(i)}(M_{i,j}^a)^2 + 2p_{1,1}^{(i)}M_{i,j}^a M_{i+1,j}^a + 2p_{0,2}^{(i)}(M_{i+1,j}^a)^2] * d\mathcal{B}_i(t).$$

280 *Proof of lemma (SM1.7).* Note that $\frac{\partial^2}{\partial s_j^2} F^{(i,a)}[s; t]|_{\mathbf{s}=1} = L_{i,j}^a(t) - M_{i,j}^a(t)$. We
281 derive (SM12) with respect to s_j and obtain:

$$282 \quad \frac{\partial^2}{\partial s_j^2} F^{(i,a)}[s; t] = \int_0^t \frac{\partial}{\partial s_j^2} f^{(i)}(F^a[s, u]) d\mathcal{B}_i(t-u) du$$

283 where

$$284 \quad \frac{\partial^2}{\partial s_j^2} f^{(i)}(F^a[s, t]) = 2p_{2,0}^{(i)} \left(F^{(i,a)}[s; t] \frac{\partial^2}{\partial s_j^2} F^{(i,a)}[s; t] + \left(\frac{\partial}{\partial s_j} F^{(i,a)}[s; t] \right)^2 \right) \\ 285 \quad + 2p_{0,2}^{(i)} \left(F^{(i+1,a)}[s; t] \frac{\partial^2}{\partial s_j^2} F^{(i+1,a)}[s; t] + \left(\frac{\partial}{\partial s_j} F^{(i+1,a)}[s; t] \right)^2 \right) \\ 286 \quad + p_{1,1}^{(i)} \left(F^{(i+1,a)}[s; t] \frac{\partial^2}{\partial s_j^2} F^{(i,a)}[s; t] + 2 \frac{\partial}{\partial s_j} F^{(i,a)}[s; t] \frac{\partial}{\partial s_j} F^{(i+1,a)}[s; t] \right. \\ 287 \quad \left. + F^{(i,a)}[s; t] \frac{\partial^2}{\partial s_j^2} F^{(i+1,a)}[s; t] \right).$$

288
289

290 When $\mathbf{s} = 1$, we get

$$291 \quad L_{i,j}^a(t) - M_{i,j}^a(t) = 2p_{2,0}^{(i)} (L_{i,j}^a - M_{i,j}^a + (M_{i,j}^a)^2) * d\mathcal{B}_i(t) \\ 292 \quad + 2p_{0,2}^{(i)} (L_{i+1,j}^a - M_{i+1,j}^a + (M_{i+1,j}^a)^2) * d\mathcal{B}_i(t) \\ 293 \quad + p_{1,1}^{(i)} (L_{i,j}^a - M_{i,j}^a + 2M_{i,j}^a M_{i+1,j}^a + L_{i+1,j}^a - M_{i+1,j}^a) * d\mathcal{B}_i(t). \\ 294 \quad 295$$

296 Using the system of equations (39), we deduce (SM14). \square

297 THEOREM SM1.8. Under the same hypotheses as in theorem 2.14, and supposing
298 that for all $i \in \llbracket 1, J \rrbracket$, $\lambda_i > 0$, we have, for all $a \geq 0$:

$$299 \quad \forall i \in \llbracket 1, J \rrbracket, \quad \forall k \in \llbracket 0, J - i \rrbracket \quad L_{i,i+k}^a(t) \sim \tilde{L}_{i,i+k}(a) e^{2\lambda_{i,i+k} t}, \quad \text{as } t \rightarrow \infty$$

300 such that

$$301 \quad \tilde{L}_{i,i}(a) = \frac{2p_{2,0}^{(i)} d\mathcal{B}_i^*(2\lambda_i) (\tilde{M}_{i,i}^a)^2}{1 - 2p_S^{(i)} d\mathcal{B}_i^*(2\lambda_i)},$$

302 and for $k \in \llbracket 1, J - i \rrbracket$,

$$303 \quad (SM15) \quad \tilde{L}_{i,i+k}(a) = \begin{cases} \frac{2p_{2,0}^{(i)} (\tilde{M}_{i,i+k}^a)^2 d\mathcal{B}_i^*(2\lambda_{i,i+k})}{1 - 2p_S^{(i)} d\mathcal{B}_i^*(2\lambda_{i,i+k})} + l_{i,i+k}(a), & \text{if } \lambda_{i,i+k} \neq \lambda_i \\ \frac{2p_{2,0}^{(i)} (\tilde{M}_{i,i+k}^a)^2 d\mathcal{B}_i^*(2\lambda_{i,i+k})}{1 - 2p_S^{(i)} d\mathcal{B}_i^*(2\lambda_{i,i+k})}, & \text{if } \lambda_{i,i+k} = \lambda_i \end{cases}$$

where

$$l_{i,i+k}(a) = \frac{[\tilde{L}_{i+1,i+k}(a) + 2p_{1,1}^{(i)} \tilde{M}_{i,i+k}^a \tilde{M}_{i+1,i+k}^a + 2p_{0,2}^{(i)} (\tilde{M}_{i+1,i+k}^a)^2] d\mathcal{B}_i^*(2\lambda_{i,i+k})}{1 - 2p_S^{(i)} d\mathcal{B}_i^*(2\lambda_{i,i+k})}.$$

304 *Proof.* Let $a \geq 0$. We introduce the following notations

$$305 \quad \widehat{L}_{i,i+k}^a(t) = L_{i,i+k}^a(t)e^{-2\lambda_{i,i+k}t}, \quad \widehat{d\mathcal{B}}_i(t) = \frac{d\mathcal{B}_i(t)}{d\mathcal{B}_i^*(2\lambda_{i,i+k})}e^{-2\lambda_{i,i+k}t}.$$

306 We use the same approach as that performed for the proof of theorem 2.14, and
307 proceed by recurrence:

$$308 \quad \mathcal{H}^k : \quad \forall i \in \llbracket 1, J-k \rrbracket, \quad L_{i,i+k}^a(t) \sim \widetilde{L}_{i,i+k}^a e^{2\lambda_{i,i+k}t}, \text{ as } t \rightarrow \infty.$$

309 When $k = 0$, according to (SM14) $L_{i,i}^a$ is solution of the renewal equation:

$$310 \quad (\text{SM16}) \quad L_{i,i}^a(t) = (1 - \mathcal{B}_i(t)) \mathbf{1}_{t \leq a} + 2p_{2,0}^{(i)}(M_{i,i}^a)^2 * d\mathcal{B}_i(t) + 2p_S^{(i)} L_{i,i}^a * d\mathcal{B}_i(t).$$

311 We rescale (SM16) by $e^{-2\lambda_i t}$ and obtain:

$$312 \quad \widehat{L}_{i,i}^a(t) = e^{-2\lambda_i t} \left[(1 - \mathcal{B}_i(t)) \mathbf{1}_{t \leq a} + 2p_{2,0}^{(i)}(M_{i,i}^a)^2 * d\mathcal{B}_i(t) \right] + 2p_S^{(i)} d\mathcal{B}_i^*(2\lambda_i) \widehat{L}_{i,i}^a * \widehat{d\mathcal{B}}_i(t).$$

313 Note that as $2\lambda_i > \lambda_i > 0$, we have $2p_S^{(i)} d\mathcal{B}_i^*(2\lambda_i) < 1$, so that we can use lemma
314 SM1.5. We compute the limit of the source term :

$$315 \quad \lim_{t \rightarrow \infty} e^{-2\lambda_i t} \left[(1 - \mathcal{B}_i(t)) \mathbf{1}_{t \leq a} + 2p_{2,0}^{(i)}(M_{i,i}^a)^2 * d\mathcal{B}_i(t) \right].$$

316 From hypothesis 2.2, we have:

$$317 \quad \int_0^\infty (1 - \mathcal{B}_i(t)) \mathbf{1}_{t \leq a} e^{-\lambda_i t} dt \leq \frac{1}{b_i} \int_0^\infty d\mathcal{B}_i(t) e^{-\lambda_i t} dt < \infty.$$

318 Thus, $(1 - \mathcal{B}_i(t)) \mathbf{1}_{t \leq a} e^{-\lambda_i t} \in \mathbf{L}^1(\mathbb{R}_+)$ and, $\lim_{t \rightarrow \infty} e^{-\lambda_i t} [1 - \mathcal{B}_i(t)] = 0$. Using the hy-
319 pothesis $\lambda_i > 0$, we obtain that $\lim_{t \rightarrow \infty} e^{-2\lambda_i t} [1 - \mathcal{B}_i(t)] = 0$. Then,

$$320 \quad e^{-2\lambda_i t} (M_{i,i}^a)^2 * d\mathcal{B}_i(t) = \int_0^\infty \mathbf{1}_{[0,t]}(M_{i,i}^a(t-u) e^{-\lambda_i(t-u)})^2 d\mathcal{B}_i(u) e^{-2\lambda_i u} du.$$

321 Using theorem 2.14, we have $M_{i,i}^a(t) \sim e^{\lambda_i t} \widetilde{M}_{i,i}(a)$, as $t \rightarrow \infty$. Applying Lebesgue
322 dominated convergence theorem, we obtain

$$323 \quad \lim_{t \rightarrow \infty} e^{-2\lambda_i t} (M_{i,i}^a)^2 * d\mathcal{B}_i(t) = (\widetilde{M}_{i,i}(a))^2 d\mathcal{B}_i^*(2\lambda_i).$$

324 Then, applying lemma SM1.5, we deduce:

$$325 \quad L_{i,i}^a(t) \sim \widetilde{L}_{i,i}(a) e^{2\lambda_i t}, \text{ as } t \rightarrow \infty, \text{ where } \widetilde{L}_{i,i}(a) = \frac{2p_{2,0}^{(i)} d\mathcal{B}_i^*(2\lambda_i) (\widetilde{M}_{i,i}(a))^2}{1 - 2p_S^{(i)} d\mathcal{B}_i^*(2\lambda_i)}.$$

326 Hence, \mathcal{H}^0 is true. Then, we suppose that \mathcal{H}^{k-1} holds and we show \mathcal{H}^k . According
327 to (SM14), we write the equation for $L_{i,i+k}^a$ and rescale it by $e^{-2\lambda_{i,i+k}t}$:

$$328 \quad \widehat{L}_{i,i+k}^a(t) = 2p_S^{(i)} d\mathcal{B}_i^*(2\lambda_{i,i+k}) \widehat{L}_{i,i+k}^a * \widehat{d\mathcal{B}}_i(t) + e^{-2\lambda_{i,i+k}t} 2p_L^{(i)} L_{i+1,i+k}^a * d\mathcal{B}_i(t) \\ 329 \quad + e^{-2\lambda_{i,i+k}t} \left[2p_{2,0}^{(i)} (M_{i,i+k}^a)^2 + 2p_{1,1}^{(i)} M_{i,i+k}^a M_{i+1,i+k}^a + 2p_{0,2}^{(i)} (M_{i+1,i+k}^a)^2 \right] * d\mathcal{B}_i(t). \\ 330 \\ 331$$

332 Here, $m = 2p_S^{(i)} d\mathcal{B}_i^*(2\lambda_{i,i+k}) < 1$, so that we can use lemma SM1.5. We first compute
 333 the limit of $e^{-2\lambda_{i,i+k}t} L_{i+1,i+k}^a * d\mathcal{B}_i(t)$ when t goes to infinity when either $\lambda_{i,i+k} = \lambda_i$
 334 or $\lambda_{i,i+k} \neq \lambda_i$. We start with the case $\lambda_{i,i+k} \neq \lambda_i$ (so, $\lambda_{i,i+k} = \lambda_{i+1,i+k}$). For all
 335 $t \geq 0$, we have:

$$336 \quad e^{-2\lambda_{i,i+k}t} L_{i+1,i+k}^a * d\mathcal{B}_i(t) =$$

$$337 \quad d\mathcal{B}_i^*(2\lambda_{i,i+k}) \int_0^\infty \mathbb{1}_{[0,t]} e^{-2\lambda_{i,i+k}(t-u)} L_{i+1,i+k}^a(t-u) \widehat{d\mathcal{B}_i}(u) du.$$

340 According to \mathcal{H}^{k-1} , we know that $L_{i+1,i+k}^a(t) \sim \widetilde{L}_{i+1,i+k}(a) e^{2\lambda_{i,i+k}t}$. We deduce with
 341 a Lebesgue dominated convergence theorem that:

$$342 \quad \lim_{t \rightarrow \infty} e^{-2\lambda_{i,i+k}t} L_{i+1,i+k}^a * d\mathcal{B}_i(t) = d\mathcal{B}_i^*(2\lambda_{i,i+k}) \widetilde{L}_{i+1,i+k}(a).$$

343 We apply the same method as above for the other terms of the source term. Theorem
 344 2.14 gives us that $M_{i,i+k}^a \sim e^{\lambda_{i,i+k}t} \widetilde{M}_{i,i+k}(a)$ and $M_{i+1,i+k}^a \sim e^{\lambda_{i,i+k}t} \widetilde{M}_{i+1,i+k}(a)$.
 345 Using Lebesgue dominated convergence theorem, we obtain:

$$346 \quad \lim_{t \rightarrow \infty} e^{-2\lambda_{i,i+k}t} \left[2p_{2,0}^{(i)} (M_{i,i+k}^a)^2 + 2p_{1,1}^{(i)} M_{i,i+k}^a M_{i+1,i+k}^a + 2p_{0,2}^{(i)} (M_{i+1,i+k}^a)^2 \right] * d\mathcal{B}_i(t)$$

$$347 \quad = \left[2p_{2,0}^{(i)} (\widetilde{M}_{i,i+k}(a))^2 + 2p_{1,1}^{(i)} \widetilde{M}_{i,i+k}(a) \widetilde{M}_{i+1,i+k}(a) \right. \\$$

$$348 \quad \left. + 2p_{0,2}^{(i)} (\widetilde{M}_{i+1,i+k}(a))^2 \right] d\mathcal{B}_i^*(2\lambda_{i,i+k}).$$

349 We then consider the case $\lambda_{i,i+k} = \lambda_i > \lambda_{i+1,i+k}$ and start by computing the
 350 limit of $e^{-2\lambda_{i,i+k}t} L_{i+1,i+k}^a * d\mathcal{B}_i(t)$.

$$351 \quad e^{-2\lambda_{i,i+k}t} L_{i+1,i+k}^a * d\mathcal{B}_i(t) =$$

$$352 \quad d\mathcal{B}_i^*(2\lambda_{i,i+k}) e^{-2(\lambda_{i,i+k} - \lambda_{i+1,i+k})t} \int_0^\infty \mathbb{1}_{[0,t]} e^{-2\lambda_{i+1,i+k}(t-u)} L_{i+1,i+k}^a(t-u) \widehat{d\mathcal{B}_i}(u) du.$$

353 Using \mathcal{H}^{k-1} and Lebesgue dominated convergence theorem, we first obtain that

$$354 \quad \lim_{t \rightarrow \infty} \int_0^\infty \mathbb{1}_{[0,t]} e^{-2\lambda_{i+1,i+k}(t-u)} L_{i+1,i+k}^a(t-u) \widehat{d\mathcal{B}_i}(u) du$$

$$355 \quad = d\mathcal{B}_i^*(2\lambda_{i+1,i+k}) \widetilde{L}_{i+1,i+k}(a) < \infty,$$

356 hence,

$$357 \quad \lim_{t \rightarrow \infty} e^{-2\lambda_{i,i+k}t} L_{i+1,i+k}^a * d\mathcal{B}_i(t) = 0.$$

358 Then, theorem 2.14 give us that $M_{i,i+k}^a \sim e^{\lambda_{i,i+k}t} \widetilde{M}_{i,i+k}(a)$ and
 359 $M_{i+1,i+k}^a \sim e^{\lambda_{i+1,i+k}t} \widetilde{M}_{i+1,i+k}(a)$. Using similar methods, we obtain:

$$360 \quad \lim_{t \rightarrow \infty} e^{-2\lambda_{i,i+k}t} \left[2p_{2,0}^{(i)} (M_{i,i+k}^a)^2 + 2p_{1,1}^{(i)} M_{i,i+k}^a M_{i+1,i+k}^a + 2p_{0,2}^{(i)} (M_{i+1,i+k}^a)^2 \right] * d\mathcal{B}_i(t)$$

$$361 \quad = 2p_{2,0}^{(i)} (\widetilde{M}_{i,i+k}(a))^2 d\mathcal{B}_i^*(2\lambda_{i,i+k}).$$

362 We conclude by applying lemma SM1.5 that \mathcal{H}^k holds. \square

371 *Variance.*

372 DEFINITION SM1.9. We write $v_j^a(t)$, the variance of $Y_t^{(j,a)}$ starting from a mother
 373 cell on the first layer such that:

374 (SM17)
$$v_j^a(t) = \mathbb{E}[(Y_t^{(j,a)})^2 | Z_0 = \delta_{1,0}] - \mathbb{E}[Y_t^{(j,a)} | Z_0 = \delta_{1,0}]^2.$$

375 We study the asymptotic behavior of the variance $v_j^a(t)$ when the first layer is the
 376 leading one.

377 COROLLARY SM1.10. Let $a \geq 0$. Under the same hypotheses as in theorem SM1.8
 378 and supposing that $c = 1$, we have

379
$$\forall k \in \llbracket 1, J \rrbracket \quad v_j^a(t) \sim \tilde{v}_j(a) e^{2\lambda_c t}, \text{ as } t \rightarrow \infty$$

380 where

381
$$\tilde{v}_j(a) = \tilde{L}_{1,j}(a) - (m_j(a))^2 = \left[\frac{2p_{2,0}^{(1)} d\mathcal{B}_1^*(2\lambda_1)}{1 - 2p_S^{(1)} d\mathcal{B}_1^*(2\lambda_1)} - 1 \right] (m_j(a))^2.$$

382 *Proof.* Let $a \geq 0$. According to theorem SM1.8 and using that $c = 1$, we have:

383
$$\forall j \in \llbracket 1, J \rrbracket, \quad L_{1,j}^a(t) \sim \tilde{L}_{1,j}(a) e^{2\lambda_1 t}, \quad \text{as } t \rightarrow \infty.$$

384 Using theorem 2.14 and SM1.8, we deduce for all $j \in \llbracket 1, J \rrbracket$:

385
$$\tilde{v}_j(a) = \tilde{L}_{1,j}(a) - (m_j(a))^2 = \left[\frac{2p_{2,0}^{(1)} d\mathcal{B}_1^*(2\lambda_1)}{1 - 2p_S^{(1)} d\mathcal{B}_1^*(2\lambda_1)} - 1 \right] (m_j(a))^2.$$

386

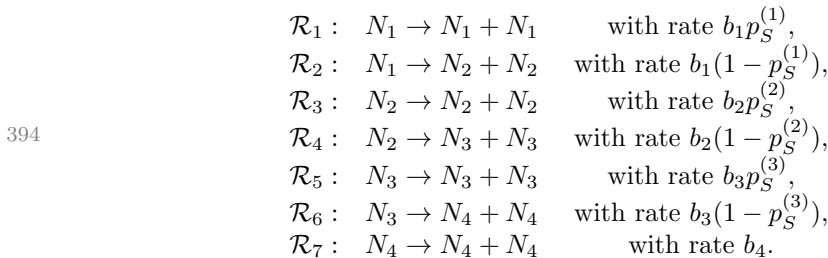
□

387 **SM2. Numerical simulation procedures.**

388 **SM2.0.1. Stochastic simulation procedures.**

389 *Markov case.* Considering a markovian case, we simulate the process Z_t solution
 390 of the SDE (2) with the Gillespie algorithm. We use the package StochSS [SM2].

391 We consider that for each layer $j \in \llbracket 1, 3 \rrbracket$, $p_{1,1}^{(j)} = 0$. Hence, $p_{2,0}^{(j)} = p_S^{(j)}$ and $p_{0,2}^{(j)} =$
 392 $1 - p_S^{(j)}$. Considering a system with 4 layers, our system is ruled by the 7-th reactions
 393 below:



395 *General case.* We simulate our process using the algorithm SM1, on a predefine
 396 time horizon T_{\max} .

Algorithm SM1 Simulation stochastic process

-
- 1: Define a sequence \mathcal{S} of cells of a given age and layer.
 - 2: Simulate the time of division of each cell in \mathcal{S}
 - 3: **while** $t < T_{\max}$ **do**
 - 4: Select the next cell m that will divide. l^m is its layer index and l^m is the age at division.
 - 5: Randomly draw the layer of its daughters cell l^{d_1} and l^{d_2} according to the probabilities $p_{2,0}^{(l^m)}$, $p_{1,1}^{(l^m)}$ and $p_{2,0}^{(l^m)}$.
 - 6: Randomly draw the next time of division of daughter cell d_1 according to its layer index l^{d_1} .
 - 7: Randomly draw the next time of division of daughter cell d_2 according to its layer index l^{d_2} .
 - 8: Add d_1 and d_2 into the sequence \mathcal{S}
 - 9: $t \leftarrow t + t^m$
 - 10: **end while**
-

397 **SM2.0.2. Deterministic simulation protocol.** To solve numerically the pro-
 398 blem (3), we design a dedicated finite volume scheme adapted to the non-conservative
 399 form with proper boundary conditions. We define the time step Δt and the age step
 400 Δa . The time discretization is defined by

$$401 \quad t_0 = 0, \quad t_{n+1} = t_n + \Delta t, \quad \text{for } n = 0, \dots, N_t$$

402 where $(N_t + 1)\Delta t$ is the time horizon of the simulation. Similarly, N_a is the number
 403 of cells¹ in the domain. The cells \mathcal{C}_i are indexed by a rational number i ($\frac{1}{2}, \frac{3}{2}$, etc.)
 404 with $i \in \llbracket \frac{1}{2}, N_a - \frac{1}{2} \rrbracket$. The edges of each cell are located at $a_{i-\frac{1}{2}} = (i - \frac{1}{2})\Delta a$ and
 405 $a_{i+\frac{1}{2}} = (i + \frac{1}{2})\Delta a$ (remark that $\Delta a = a_{i+\frac{1}{2}} - a_{i-\frac{1}{2}}$ and $a_0 = 0$). As age and time
 406 evolve at the same speed, we chose N_a such that $t_{N_t} - a_{\max}^0 < N_a \Delta a$ where a_{\max}^0 is
 407 the maximal age of the initial distribution.

408
 409 Let $j \in \llbracket 1, J \rrbracket$. We define $P_{n,i}^j$ as the mean value of the density $\rho^{(j)}$ in cell \mathcal{C}_i at
 410 time t_n :

$$411 \quad P_{n,i}^j := \frac{1}{\Delta a} \int_{a_{i-\frac{1}{2}}}^{a_{i+\frac{1}{2}}} \rho^{(j)}(t_n, a) da.$$

412 We integrate the equation $\partial_t \rho^{(j)} + \partial_a \rho^{(j)} = -b_j \rho^{(j)}$ with respect to age in cell \mathcal{C}_i and
 413 obtain:

$$414 \quad \frac{d}{dt} \int_{a_{i-\frac{1}{2}}}^{a_{i+\frac{1}{2}}} \rho^{(j)}(t, a) da = -\rho^{(j)}(t, a_{i+\frac{1}{2}}) + \rho^{(j)}(t, a_{i-\frac{1}{2}}) - \int_{a_{i-\frac{1}{2}}}^{a_{i+\frac{1}{2}}} b_j(a) \rho^{(j)}(t, a) da.$$

415 Then, we suppose that all b_j s functions are regular enough so that we can approximate
 416 b_j , for all $j \in \llbracket 1, J \rrbracket$ on each cell \mathcal{C}_i by their mean value \bar{b}_j^i . We obtain:

$$417 \quad \frac{d}{dt} \int_{a_{i-\frac{1}{2}}}^{a_{i+\frac{1}{2}}} \rho^{(j)}(t, a) da = -\rho^{(j)}(t, a_{i+\frac{1}{2}}) + \rho^{(j)}(t, a_{i-\frac{1}{2}}) - \bar{b}_j^i \int_{a_{i-\frac{1}{2}}}^{a_{i+\frac{1}{2}}} \rho^{(j)}(t, a) da.$$

¹The cell is here the standard name used for each elementary volume in the framework of finite volume methods.

418 We approximate the derivative in time with a finite difference scheme:

$$419 \quad \frac{d}{dt} \int_{a_{i-\frac{1}{2}}}^{a_{i+\frac{1}{2}}} \rho^{(j)}(t_n, a) da = \frac{1}{\Delta t} \left[\int_{a_{i-\frac{1}{2}}}^{a_{i+\frac{1}{2}}} \rho^{(j)}(t_{n+1}, a) da - \int_{a_{i-\frac{1}{2}}}^{a_{i+\frac{1}{2}}} \rho^{(j)}(t_n, a) da \right] + \mathcal{O}(\Delta t)$$

420 and we deduce:

$$421 \quad \frac{\Delta a}{\Delta t} \left[P_{n+1,i}^j - P_{n,i}^j \right] = -\rho^{(j)}(t, a_{i+\frac{1}{2}}) + \rho^{(j)}(t, a_{i-\frac{1}{2}}) - \bar{b}_i^j \Delta a P_{n,i}^j.$$

422 The edge terms $\rho^{(j)}(t, a_{i+\frac{1}{2}})$ and $\rho^{(j)}(t, a_{i-\frac{1}{2}})$ correspond to the fluxes that cross the
 423 boundaries of cell \mathcal{C}_i . When $i = \frac{1}{2}$, the boundary condition of equation (3) gives us
 424 the value of this term:

$$425 \quad \rho^{(j)}(t_n, a_0) = 2p_S^{(j)} \int_0^\infty b_j(a) \rho^{(j)}(t_n, a) da + 2(1 - p_S^{(j-1)}) \int_0^\infty b_{j-1}(a) \rho^{(j-1)}(t_n, a) da$$

$$426 \quad = 2p_S^{(j)} \sum_i \int_{\mathcal{C}_i} b_j(a) \rho^{(j)}(t_n, a) da + 2(1 - p_S^{(j-1)}) \sum_i \int_{\mathcal{C}_i} b_{j-1}(a) \rho^{(j-1)}(t_n, a) da$$

$$427 \quad = 2p_S^{(j)} \Delta t \sum_i \bar{c}_i P_{n,i}^j + 2(1 - p_S^{(j-1)}) \Delta t \sum_i \bar{c}_i^{j-1} P_{n,i}^{j-1}.$$

428

429

430

431 When $i \neq \frac{1}{2}$, we approximate each term $\rho^{(j)}(t_n, a_{i+\frac{1}{2}})$ by

$$432 \quad \rho^{(j)}(t_n, a_{i+\frac{1}{2}}) = P_{n,i+\frac{1}{2}}^j + \mathcal{O}(\Delta a).$$

433 Hence, we obtain the following numerical scheme:

$$434 \quad P_{n+1,i}^j = \left[1 - \bar{b}_i^j \Delta t - \frac{\Delta t}{\Delta x} \right] P_{n,i}^j + \frac{\Delta t}{\Delta x} P_{n,i-1}^j$$

435

$$436 \quad P_{n+1,\frac{1}{2}}^j = \left[1 - \bar{c}_{\frac{1}{2}}^j \Delta t - \frac{\Delta t}{\Delta x} \right] P_{n,\frac{1}{2}}^j + 2s_j \Delta t \sum_i \bar{c}_i P_{n,i}^j + 2(1 - s_{j-1}) \Delta t \sum_i \bar{c}_i^{j-1} P_{n,i}^{j-1}.$$

437 **SM2.1. Construction of figure 4.** In this part, we give some details about the
 438 construction of figure 4. We simulate the SDE (2) using the algorithm SM1 and the
 439 PDE (3) using the algorithm described in the subsection below (see SM2.0.2) taking
 440 $\Delta a = 9.5 \times 10e - 3$ and $\Delta t = 10e - 4$.

441 We discretized the age according to a sequence of integers $k \in \llbracket 1, 50 \rrbracket$. Let
 442 $j \in \llbracket 1, J \rrbracket$ be a layer index. The color bar associated with age k for the j -th layer cor-
 443 responds to the total number of cells on the j -th layer of age $a \in [k, k+1[$ renormalized
 444 by the total number of cells:

$$445 \quad \frac{\langle\langle Z_t, \mathbb{1}_{j,k \leq a < k+1} \rangle\rangle}{\langle\langle Z_t, \mathbb{1} \rangle\rangle}.$$

446 The dashed black line with the age k for the j -th layer corresponds to:

$$447 \frac{\int_k^{k+1} \rho^{(j)}(t, a) da}{\sum_{j=1}^4 \int_0^{+\infty} \rho^{(j)}(t, a) da} \sim \frac{\sum_{i=\lfloor \frac{k}{\Delta x} \rfloor}^{\lfloor \frac{k+1}{\Delta x} \rfloor - 1} P_{n,i}^j}{\sum_{j=1}^4 \sum_i P_{n,i}^j}.$$

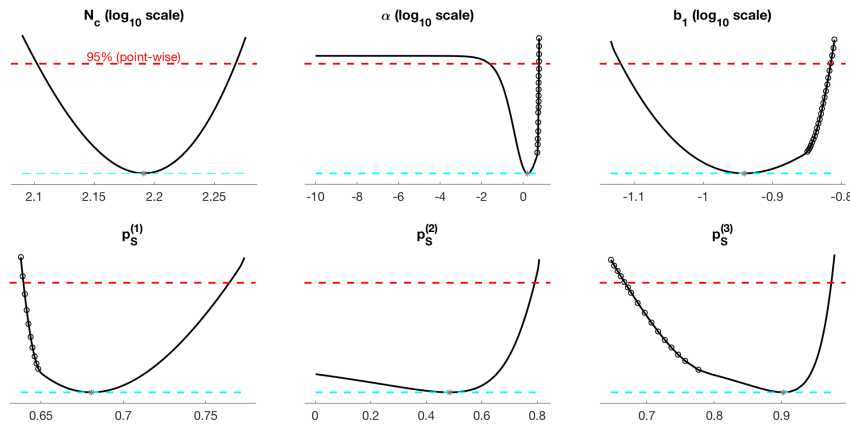
448 The color solid lines which represent the stable distribution $\hat{\rho}$ and compute their
449 value at each age point k by

$$450 \frac{\int_k^{k+1} \hat{\rho}^{(j)}(a) da}{\sum_{j=1}^4 \int_0^{+\infty} \hat{\rho}^{(j)}(a) da}.$$

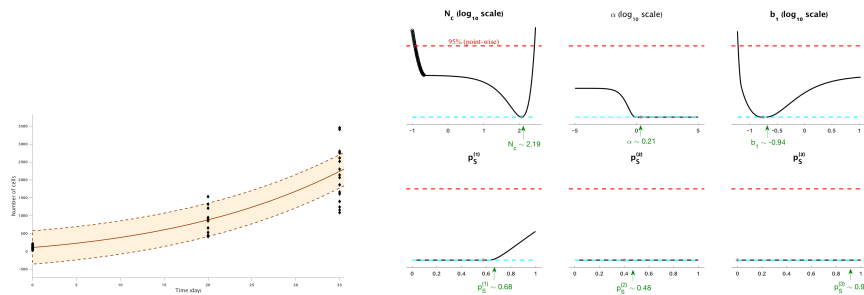
451 **SM2.2. Parameter estimation procedure.** Using the software D2D [SM7],
452 we estimate the parameters of our model, using an additive Gaussian noise statistical
453 model (standard least squares likelihood). The standard deviation and the initial
454 number N of cells on the first layer are also estimated. To investigate the practical
455 identifiability, we compute the profile likelihood estimate (PLE) [SM6]. We observe
456 that all the parameters are practically identifiable except the probability of staying on
457 the second layer $p_S^{(2)}$ (see Figure SM1a). In contrast, most of the parameters are not
458 practically identifiable when we consider the total number of cells as the observable
459 function ($\sigma(t; p) = \sum_{j=1}^J M^{(j)}(t; p)$, Figure SM1b).

460 REFERENCES

- 461 [SM1] N. CHAMPAGNAT, R. FERRIÈRE, AND S. MÉLÉARD, From Individual Stochastic Processes
462 to Macroscopic Models in Adaptive Evolution, *Stoch. Models*, 24 (2008), pp. 2–44, <https://doi.org/10.1080/15326340802437710>.
463
464 [SM2] B. DRAWERT, A. HELLANDER, B. BALES, D. BANERJEE, G. BELLESIA, B. J. D. JR, G. DOU-
465 GLAS, M. GU, A. GUPTA, S. HELLANDER, C. HORUK, D. NATH, A. TAKKAR, S. WU,
466 P. LÖTSTEDT, C. KRINTZ, AND L. R. PETZOLD, Stochastic Simulation Service: Bridging
467 the Gap between the Computational Expert and the Biologist, *PLoS Comput. Biol.*, 12
468 (2016), p. e1005220, <https://doi.org/10.1371/journal.pcbi.1005220>.
469 [SM3] T. E. HARRIS, The theory of branching processes, Springer-Verlag, 1963.
470 [SM4] F. C. KLEBANER, Introduction to stochastic calculus with applications, Imperial College Press,
471 3 ed., 2012.
472 [SM5] P. E. PROTTER, Stochastic Integration and Differential Equations, Springer, 2nd ed., 2004.
473 [SM6] A. RAUE, C. KREUTZ, T. MAIWALD, J. BACHMANN, M. SCHILLING, U. KLINGMÜLLER, AND
474 J. TIMMER, Structural and practical identifiability analysis of partially observed dynamical
475 models by exploiting the profile likelihood, *Bioinformatics*, 25 (2009), pp. 1923–1929, <https://doi.org/10.1093/bioinformatics/btp358>.
476
477 [SM7] A. RAUE, B. STEIERT, M. SCHELKER, C. KREUTZ, T. MAIWALD, H. HASS, J. VANLIER,
478 C. TÖNSING, L. ADLUNG, R. ENGRESSER, W. MADER, T. HEINEMANN, J. HASENAUER,
479 M. SCHILLING, T. HÖFER, E. KLIPP, F. THEIS, U. KLINGMÜLLER, B. SCHÖBERL, AND
480 J. TIMMER, Data2dynamics: a modeling environment tailored to parameter estimation
481 in dynamical systems, *Bioinformatics*, 31 (2015), pp. 3558–3560, [https://doi.org/10.1093/](https://doi.org/10.1093/bioinformatics/btv405)
482 [bioinformatics/btv405](https://doi.org/10.1093/bioinformatics/btv405).
483 [SM8] V. C. TRAN, Modèles particuliers stochastiques pour des problèmes d'évolution adaptative
484 et pour l'approximation de solutions statistiques, PhD thesis, Université de Nanterre-Paris
485 X, 2006.



(a) Practical Identifiability for $\sigma(t; p) = (M^{(j)}(t; p))_{j \in [1, J]}$



(b) Practical Identifiability for $\sigma(t; p) = \sum_{j=1}^J M^{(j)}(t; p)$

FIGURE SM1. **Practical Identifiability.** **Figure SM1a** Profile likelihood estimate (PLE) for each parameter in the set $\mathbf{P}_{exp} = \{N, b_1, \alpha, p_S^{(1)}, p_S^{(2)}, p_S^{(3)}\}$ when the observation function is $\sigma(t; p) = (M^{(j)}(t; p))_{j \in [1, J]}$. The red dashed lines correspond to the 95%-statistical threshold while the blue dashed lines correspond to the optimum value of the likelihood. **Figure SM1b** Parameter estimation results for $\sigma(t; p) = \sum_{j=1}^J M^{(j)}(t; p)$. **Left panel:** Data fitting model with model (8). The black diamonds represent the experimental data (total number of cells), the solid line is the best fit solution of (8) and the dashed lines are drawn from the estimated variance. **Left panel:** Profile likelihood estimates of each parameter in the set \mathbf{P}_{exp} .

Comment citer ce document :