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Applications of Environment-Dependent Models to Tumor Immunity

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環境依存型モデルの腫瘍免疫への応用

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We consider an environment-dependent spatial model. This random model is related to the stochastic interacting system. We shall show that rescaled processes converge to a Dawson-Watanabe superprocess. Formulation is due to setup of measure-valued branching Markov processes. The first step toward a transformation of model into a superprocess is based upon construction of empirical meaures. Moreover, we discuss the applicational issues of our random model to tumor immunity.

本研究では環境依存型の空間モデルを考察する．このランダム・モデルは確率相互作用系と深いつながりがあるものである．この報告の中では，スケール変換された確率モデルがドーソン＝渡辺超過程に収束することが示される．この収束の定式化は測度値分枝マルコフ過程の枠組みにおいてなされる．環境依存型モデルから超過程への変換の最初のステップは経験測度の構成に基づいている．さらに構成された確率モデルの腫瘍免疫応答への応用について議論する．

1 Environment-dependent formalism

When $\mathbb{Z}^d$ is a d-dimensional lattice, we suppose that each site on $\mathbb{Z}^d$ is occupied by either one of the two species. At each random time, a particle dies and is replaced by a new one, but the random time and the type chosen of the species are assumed to be determined by the environment conditions around the particle. The random function $\eta_t : \mathbb{Z}^d \to \{0,1\}$ denotes the state at time t, and each number of $\{0,1\}$ denotes the label of the type chosen of the two species. We define $\mathcal{N}_x := x + \{y : 0 < \|y\|_\infty \leqslant r\}$ as an r-neighborhood of x. For $i = 0,1$, let $f_i(x,\eta)$ be a frequency of appearance of type i in $\mathcal{N}_x$ for η. In other words,

$$f_i(x) \equiv f_i(x,\eta) := \frac{\#\{y : \eta_t(y) = i \; ; \; y \in \mathcal{N}_x\}}{\#\mathcal{N}_x}. \tag{1}$$

For non-negative parameters $\alpha_{ij} \geq 0$, the dynamics of η_t is defined as follows. The state η makes transition $0 \to 1$ at rate $\lambda f_1(f_0+\alpha_{01}f_1)/(\lambda f_1+f_0)$, and it makes transition $1 \to 0$ at rate $f_0(f_1+\alpha_{10}f_0)/(\lambda f_1+f_0)$. The particle of type i dies at rate $f_i + \alpha_{ij}f_j$, and is replaced instantaneously by either one of the two species chosen at random, according to the proliferation rate of type 0 and the interaction (= the competitive result) with the particle of type 1. The density-dependent death rate $f_i + \alpha_{ij}f_j$ consists of the intraspecific and interspecific competitive effects [8]. We assume that competitive two species possess the same intensity of intraspecific interaction. The exchange of particles after death is described in the form being proportional to the weighted density between the two species, expressed by a parameter λ. Assume that $\lambda \geq 1$.

2 Scaling rule

For brevity's sake we shall treat a case $\lambda = 1$ only. For $N = 1,2,\ldots$, let $m_N \in \mathbb{N}$, and we put $\ell_N := m_N\sqrt{N}$, and $\mathbb{S}_N := \mathbb{Z}^d/\ell_N$, and $W_N = (W_N^1, \ldots, W_N^d) \in (\mathbb{Z}^d/M_N) \setminus \{0\}$ is defined as a random vector satisfying (i) $\mathcal{L}(W_N) = \mathcal{L}(-W_N)$; (ii) $E(W_N^iW_N^j) \to \delta_{ij}\sigma^2(\geq 0)$ (as $N \to \infty$); (iii) $\{|W_N|^2\}$ $(N \in \mathbb{N})$ is uniformly integrable. Here $\mathcal{L}(Y)$ indicates the law of a random variable Y. For the kernel

$p_N(x) := P(W_N/\sqrt{N} = x)$, $x \in \mathbb{S}_N$ and $\eta \in \{0,1\}^{\mathbb{S}_N}$, we define the scaled frequency f_i^N as

$$f_i^N(x,\eta) = \sum_{y \in \mathbb{S}_N} p_N(y-x) 1_{\{\eta(y)=i\}}, \qquad (i = 0,1). \tag{2}$$

We denote by η_t^N the state determined by the scaled frequency depending on α_i^N and p_N. As a matter of fact, the rescaled process $\eta_t^N : \mathbb{S}_N \ni x \mapsto \eta_t^N(x) \in \{0,1\}$ is determined by the following state transition law, nemaly, it makes transition $0 \to 1$ at rate $Nf_1^N(f_0^N + \alpha_0^N f_1^N)$, or else it makes transition $1 \to 0$ at rate $Nf_0^N(f_1^N + \alpha_1^N f_0^N)$. The symbol $Res(p_N, \alpha_i^N)$ denotes the rescaled process η_t^N.

3 Superprocess via variational derivative approach

On this account, we may define the associated measure-valued process (or its corresponding empirical measure) as

$$X_t^N := \frac{1}{N} \sum_{x \in \mathbb{S}_N} \eta_t^N(x) \delta_x. \tag{3}$$

For the initial value X_0^N, we assume that $\sup_N \langle X_0^N, 1 \rangle < \infty$, and $X_0^N \to X_0$ in $M_F(\mathbb{R}^d)$ (as $N \to \infty$), where $M_F(\mathbb{R}^d)$ is the totality of all the finite measures on $\mathbb{R}^d$, equipped with the topology of weak convergence. Let $\Omega_D := D([0,\infty), M_F(\mathbb{R}^d))$ be the Skorokhod space of all the $M_F(\mathbb{R}^d)$-valued cadlag paths, and $\Omega_C := C([0,\infty), M_F(\mathbb{R}^d))$ be the space of all the $M_F(\mathbb{R}^d)$-valued continuous paths, equipped with uniform convergence topology on compacts. On the other hand, the first order variational derivative of a function F on $M_F(E)$ relative to $\mu \in M_F(E)$ is defined as

$$\frac{\delta F(\mu)}{\delta \mu(x)} = \lim_{r \to 0+} \frac{F(\mu + r \cdot \delta_x) - F(\mu)}{r}, \qquad (x \in E) \tag{4}$$

if the limit in the right-hand side of (4) exists. In addition, the second order variational derivative $\delta^2 F(\mu)/\delta\mu(x)^2$ is defined as the first order variational derivative of $G(\mu) = \delta F(\mu)/\delta\mu(x)$ if its limit exists. We define the generator $\mathcal{L}_0$ as

$$\mathcal{L}_0 F(\mu) := \int_E A \frac{\delta F(\mu)}{\delta \mu(x)} \mu(dx) + \int_E \gamma \frac{\delta^2 F(\mu)}{\delta \mu(x)^2} \mu(dx), \tag{5}$$

where $A[\cdot] = \frac{\sigma^2}{2}\Delta[\cdot] + \theta[\cdot]$ and $\gamma > 0$. If $M_F(E)$-valued continuous stochastic process $X = \{X_t, P_\eta\}$ is a solution to the $(\mathcal{L}_0, \mathrm{Dom}(\mathcal{L}_0))$-martingale problem, then $X = \{X_t, P_\eta\}$ is called a Dawson-Watanabe superprocess, or DW superprocess in short, where $2\gamma \geq 0$ is a branching rate, $\theta \in \mathbb{R}$ is a drift term and $\sigma^2 > 0$ is a diffusion coefficient.

4 Assumptions

Let $\{\xi_t^x\}$ be a continuous time random walk with rate N and step distribution p_N starting at a point $x \in \mathbb{S}_N$, and $\{\hat{\xi}_t^x\}$ be a continuous time coalescing random walk with rate N and step distribution p_N starting at a point x. For a finite set $A \subset \mathbb{S}_N$, we denote by $\tau(A)$ the time when all the particles starting from A finally coalesce into a single particle. Take a sequence $\{\varepsilon_N\}$ of positive numbers such that $\varepsilon_N \to 0$ and $N\varepsilon_N \to \infty$ as $N \to \infty$. Moreover, we suppose that when $N \to \infty$,

$$N \cdot P(\xi_{\varepsilon_N}^0 = 0) \to 0 \quad \text{and} \quad \sum_{e \in \mathbb{S}_N} p_N(e) \cdot P(\tau(\{0,e\}) \in (\varepsilon_N, t]) \to 0 \quad (\forall t > 0). \tag{6}$$

We also assume that the following limits exist :

$$\lim_{N \to \infty} \sum_{e \in \mathbb{S}_N} p_N(e) \cdot P(\tau(\{0,e\}) > \varepsilon_N) = \exists\gamma(>0) \quad \text{and} \quad \lim_{N \to \infty} P\left(\tau(A/\ell_N) \leqslant \varepsilon_N\right) = \exists\zeta(A) \tag{7}$$

holds for any finite subset $A \subset \mathbb{Z}^d$. We also denote by S_F the totality of all the finite subsets in $\mathbb{Z}^d$.

5 Perturbation

According to [10], we consider decomposing proper components of our model $Res(p_N, \alpha_i^N)$ into two parts; a part of the principal interacting particle system and the other part. Based upon the notation in [11], we consider decomposing the rate function $c_N(x,\eta)$. In fact, we shall rewrite first a rate $Nf_i^N(f_j^N + \alpha_j^N f_i^N)$ into a new rate $Nf_i^N + \theta_j^N(f_i^N)^2$ by using a relation $\theta_i^N = N(\alpha_i^N - 1)$, and next decompose the rate function $c_N(x,\eta)$ (which changes the coordinate $\eta(x)$ into $1-\eta(x)$) as $c_N(x,\eta) = N \cdot c_0(x,\eta) + c_p(x,\eta) \geq 0$, where $c_0(x,\eta) := \sum_{e \in \mathbb{S}_N} p_N(e) 1_{\{\eta(x+e) \neq \eta(x)\}}$, and

$$\begin{aligned} c_p(x,\eta) &:= \theta_0^N (f_1^N(x,\eta))^2 1_{\{\eta(x)=0\}} + \theta_1^N (f_0^N(x,\eta))^2 1_{\{\eta(x)=1\}} \\ &= \sum_{A \in S_F} \Big(\prod_{e \in A/\ell_N} \eta(x+e)\Big)(\beta_N(A) 1_{\{\eta(x)=0\}} + \delta_N(A) 1_{\{\eta(x)=1\}}). \end{aligned} \tag{8}$$

On the assumption that for real-valued functions β_N and δ_N defined on S_F, there exist proper real-valued functions β and δ defined on S_F such that $\beta_N \to \beta$ and $\delta_N \to \delta$ are valid for each point of S_F as $N \to \infty$, we consider the convergence of the law of the empirical measure X^N. For simplicity, when we set

$$F_1(S_F) := \{f : S_F \to \mathbb{R};\ \|f\|_1 := \sum_{A \in S_F} |f(A)| < \infty\}, \tag{9}$$

then it follows that $\beta_N(\cdot)\zeta_N(\cdot) \to \beta(\cdot)\zeta(\cdot)$ in $F_1(S_F)$ as $N \to \infty$. While, when we define

$$\theta^1(\beta, \zeta(\cdot)) := \sum_{A \in S_F} \beta(A)\zeta(A), \quad \theta^2(\beta,\delta,\zeta(\cdot)) := \sum_{A \in S_F} (\beta(A) + \delta(A))\zeta(A \cup \{0\}), \tag{10}$$

then we put $\theta = \theta^1(\beta, \zeta(\cdot)) - \theta^2(\beta, \delta, \zeta(\cdot))$.

6 Convergence result

THEOREM 1. (cf. [1]) *When we denote the law of a measure-valued stochastic process X^N on the path space Ω_D by P_N, then there exists a probability measure $P^* \in \mathcal{P}(\Omega_C)$ such that*

$$P_N \quad \Longrightarrow \quad P^*_{X_0} \qquad (\text{as} \quad N \to \infty). \tag{11}$$

Then there exists a $M_F(\mathbb{R}^d)$-valued stochastic process $X_t = X_t^{2\gamma,\theta,\sigma^2}$ named a DW superprocess with parameters $2\gamma > 0$, $\theta \in \mathbb{R}$ and $\sigma^2 > 0$, satisfying that X_t^N converges to $X_t^{2\gamma,\theta,\sigma^2}$ as $N \to \infty$ in the sense of weak convergence for measures, and $P^*_{X_0}$ is the law of $X_t^{2\gamma,\theta,\sigma^2}$.

Then we attain that

$$\int_0^t f'(X_s(\varphi))dM_s(\varphi) = f(\langle X_t, \varphi\rangle) - f(\langle X_0, \varphi\rangle) - \int_0^t f'(X_s(\varphi))\langle X_s, A\varphi\rangle ds - \int_0^t f''(X_s(\varphi))\langle X_s, \gamma\varphi^2\rangle ds \tag{12}$$

is a continuous, $\mathcal{F}_t^X$-measurable, L^2-martingale. Equivalently, for $F(\mu) = f(\langle \mu, \varphi\rangle)$ with $F \in \mathrm{Dom}(\mathcal{L}_0)$,

$$F(X_t) - F(X_0) - \int_0^t \mathcal{L}_0 F(X_s)ds \quad \text{is a} \quad P^*_{X_0} - \text{martingale}.$$

As a consequence, it is proven that the law $P(X_\cdot \in (\cdot))$ of the limit process $X = \{X_t\}$ satisfies the martingale problem characterizing $P^*_{X_0} \in \mathcal{P}(\Omega_C)$.

7 Sketch of proof

Based on the estimation $E[\ \sup_{0 \leqslant t \leqslant T} |\eta_t^N|^2\ ] < \infty$ for $\forall T > 0$, combining the discussion on death and birth processes to a series of results for voter models [10] together, the first decomposition for rescaled process models $Res(p_N, \alpha_i^N)$ holds, i.e.

$$\eta_t^N(x) = \eta_0^N(x) + M_t^{N,x} + D_t^{N,x}, \qquad \forall x \in \mathbb{S}_N, t \geq 0, \tag{13}$$

where $M_t^{N,x}$ is a square integrable orthogonal martingale, and its predictable quadratic variation process is given by

$$\langle M^{N,x}\rangle_t = \int_0^t \{\sum_y N \cdot p_N(y-x)(\xi_s^N(y) - \xi_s^N(x))^2 + \sum_A (\prod_e \xi_s^N(x+e))(\beta_N(A)1_{\{\xi_s^N(x)=0\}} + \delta_N(A)1_{\{\xi_s^N(x)=1\}})\}ds. \tag{14}$$

Moreover, the term $D_t^{N,x}$ is given by

$$D_t^{N,x} = \int_0^t \{\sum_y N \cdot p_N(y-x)(\xi_s^N(y) - \xi_s^N(x)) + \sum_A (\prod_e \xi_s^N(x+e))(\beta_N(A)1_{\{\xi_s^N(x)=0\}} - \delta_N(A)1_{\{\xi_s^N(x)=1\}})\}ds. \tag{15}$$

Here the variable y runs over $\mathcal{S}_N$ and A does over S_F in the above estimation $\sum$ of (14), (15), and e runs over the set A/ℓ_N in the above product $\prod$. Next, by employing Itô's formula and applying the decomposition theorem for semimartingales to η_t^N, for any $\varphi \in C_b([0,T] \times \mathbb{S}_N)$ and $0 \leqslant t \leqslant T$, X_t^N permits the following second decomposition

$$\langle X_t^N, \varphi_t\rangle = \langle X_0^N, \varphi_0\rangle + D_t^N(\varphi) + M_t^N(\varphi), \tag{16}$$

where $M_t^N(\varphi)$ is a square integrable martingale. Then, based upon the relative compactness for the law $\{P_N\}$ of $X^N_\cdot$, we take the limit procedure. It suffices to check whether all the weakly convergent limit points $X_\cdot$ of subsequence $X_\cdot^{N(k)}$ satisfy the martingale problem that characterizes the superprocess with designated parameters $(2\gamma, \theta, \sigma^2)$. For more details, see e.g. [9].

8 Terminology

Let X_t be a superprocess obtained in Theorem 1 in §6, namely, it is a measure-valued branching Markov process. If $\langle X_t, 1\rangle > 0$ holds for any time $t \geq 0$, then it is said that X_t *survives* or is *existent*. Medically or biologically, that just corresponds to the situation where both normal cells and cancer cells are coexistent. On the contrary, X_t is said to be *extinct* if the equality $\langle X_t, 1\rangle = 0$ holds for $\forall t > T$ with sufficiently large time $T > 0$. This means that it dies out after a certain amount of time passed. So that, medically or biologically, it means that it becomes cancerous in a clinical sense. Next X_t is said to exhibit *local extinction* if there exists a proper random time $\zeta_B(\omega)$ for each bounded subset B given, such that $X_t(B) = 0$ holds for $\forall t \geq \zeta_B(\omega)$. This implies that X_t can be extinct if we look at it locally. Medically or biologically, cancer cells are stronger than effector group (immune cells) and cancer cells have a tendency of occupying more and more regions [2], [3]. This is very important concept on an applicational basis. On the other hand, X_t is said to exhibit *finite time extinction* [6] if $P_\mu(X_t = 0 \text{ for } \forall t \geq T) = 1$ holds for $\exists$ some $T > 0$. This means that X_t necessarily dies out in a finite time, and can never survive. Hence, medically or biologically, it showing a tendency to be cancerous.

9 Extinction and tumor immune effect

For the superprocess obtained in Theorem 1, in the case of $d \geq 3$, the sufficient condition for long-time survival phenomena to occur is $\theta > 0$ for the drift parameter θ of the process X_t. In other words, when the inequality $\theta^1 > \theta^2$ holds (cf. Eq.(10) in §5), then long-time existence of X_t can be guaranteed. This is nothing but providing the guarantee of existence of normal cells [5]. For the case of reverse inequality $\theta^1 < \theta^2$, the long-time existence of X_t is not valid (Table 1). For simplicity, we set $P^* := P_{X_0}^{2\gamma,\theta,\sigma^2} = \mathcal{L}(X_t^{2\gamma,\theta,\sigma^2})$. Since (X_t, P^*) is a measure-valued branching Markov process, generally speaking, according

$\theta > 0$ ($\theta^1 > \theta^2$)	X_t : existent for a long time (possible to become coexistent with cancers
$\theta < 0$ ($\theta^1 < \theta^2$)	X_t : not alive for a long time (tendency to become cancerous finally

表 1 Existence of superprocess X_t.

to the property of Markov process that governs random behaviors, (i) it dies out locally (local extinction); (ii) it completely vanishes (finite time extinction); (iii) it converges to a stationary state as the time goes by (Table 2).

More precisely, for the case of $d = 1$, the process X_t is always extinct locally, and it is in a cancerous situation with probability one. For the case of $d \geq 2$, it exposes distinct phenomena according to the conditions. Those conditions are stated in terms of operator analysis, however the result turns out to be distinct in accordance with the property of Markov process, because after all the generator (=differential operator) just corresponds to Markov process itself by one-to-one. When we denote by H_θ^+ the class of positive harmonic functions, then we have

$$H_\theta^+ := \{u \in C^2 : \ u > 0, \ (L+\theta)u = 0 \quad \text{on} \quad \mathbb{R}^d\}. \tag{17}$$

The (EF) condition (resp. (DH) condition) is given by the followings respectively:

(EF) $\exists h \in C^{2,\varepsilon}$ (Hölder), $\quad 0 < \varepsilon < 1; \quad \exists B \subset \mathbb{R}^d \quad$ such that
$\inf_x \gamma h > 0 \quad$ and $\quad (L+\theta)h \leqslant 0 \quad$ on $\quad \mathbb{R}^d \setminus \bar{B}$.

(DH) $\exists c > 0 \quad$ such that $\quad (X_t, P_{c\lambda}) \quad$ converges weakly to $\quad Y_c \in \mathcal{P}(M_F(\mathbb{R}^d))$,

$d = 1$	total mass process $\langle X_t, 1\rangle$	no condition	finite time extinction (cancerous with probability one)
$d = 1$	superprocess X_t	no condition	local extinction (tendency to become cancerous)
$d \geq 2$	superprocess X_t	$H_\theta^+ \neq \emptyset$	local extinction (tendency to become cancerous)
$d \geq 2$	superprocess X_t	(EF) condition	finite time extinction (cancerous)
$d \geq 2$	superprocess X_t	(DH) condition	stationary state

表 2 Extinction property of superprocess X_t.

where λ denotes the Lebegue measure on $\mathbb{R}^d$. If $H_\theta^+ \neq \emptyset$, then we can say that it is showing medically a tendency of being cancerous, since the local extinction holds there. Besides, under the (EF) condition, it exposes finite time extinction, and it implies that it is in a cancerous situation. Under (DH) condition, it proves to be in a stationary state.

10 Mathematical analysis

In this section we shall prove mathematical statements which are used in the previous section to explain some applications of random models to immune response against cancer cells.

THEOREM 2. (Local extinction) *The DW superprocess X_t exhibits local extinction if and only if there exists a strictly positive solution $u > 0$*, i.e., $u \in H_\theta^+$.

Proof. Recall Pinsky's criticality theory for superdiffusion [12]. Let λ_c denote the generalized principal eigenvalue for $L = \frac{\sigma^2}{2}\Delta$ on $\mathbb{R}^d$ with $d \geq 2$. We shall show that if $\theta \leqslant -\lambda_c$, then X_t exhibits local extinction. Thanks to Iscoe (1988)'s argument for super-Brownian motions, for a ball B_R of radius $R > 0$, we readily get

$$P_\mu(\int_t^\infty X_s(B_R)ds = 0) = \lim_{n\to\infty} \exp(-\int v_n(t,x)\mu(dx)), \tag{18}$$

where v_n is the unique solution in $C_0(\mathbb{R}^d)$ to the evolution equation $\partial_t u = Lu + \theta u - \alpha u^2$ on $[0,\infty) \times \mathbb{R}^d$ with the minimal positive solution $u(0,x) = \phi_n(x)$ to $Lv + \theta v - \alpha v^2 + \psi_n = 0$ with a proper test function ψ_n (cf. (1.5) of [12]). On this account, we have only to verify that $\lim_{t\to\infty}\lim_{n\to\infty} v_n(t,x) = 0$. The classical parabolic maximum principle leads to $v_n(t,x) \leqslant \beta/\{\alpha(1-e^{-\beta t})\}$ for $\forall x \in \mathbb{R}^d$, $t > 0$ and $\forall n$. Hence, by monotone property in n we obtain

$$v(t,x) := \lim_{n\to\infty} v_n(t,x) < \infty, \qquad \forall x \in \mathbb{R}^d, \quad t > 0. \tag{19}$$

So that, to complete the proof, it suffices to show that $w(x) := \lim_{t\to\infty} v(t,x) = 0$. By employing the uniqueness of the solution v_n, and taking advantage of the expression for local martingale

$$v_n(t-s, Y_s) - \int_0^s (\alpha v_n^2 - \beta v_n)(t-r, Y_r)dr \tag{20}$$

(where Y_s is a diffusion process corresponding to the operator L), we may apply the fundamental property of subcritical operators to obtain

$$v_m(x) = E_x[v_m(Y_{\sigma_{n_0}}) \cdot \exp\{\int_0^{\sigma_{n_0}} (\beta - \alpha v_m)(Y_t)dt\} : \quad \sigma_{n_0} < \tau_m] \tag{21}$$

for $x \in B_m \setminus B_{n_0}$ with $\sigma_{n_0} := \inf\{t \geq 0 : |Y_t| \leqslant n_0\}$ and $\tau_m := \inf\{t \geq 0 : |Y_t| \geq m\}$, where we made use of the functional analytic argument related to the Green function G for $L + \beta - \alpha\phi$. On the assumption that $w > 0$, leading to a contradiction completes the proof, by employing the discussion on the cone of positive harmonic functions on $\mathbb{R}^d$ for the operator $L + \beta - \alpha w$. □

Recall one of the definition for extinction. We say that X_t exhibits *weak local extinction* under P_μ if for every Borel set $B \subset\subset D$, $P_\mu(\lim_{t\to\infty} \|X_t\| = 0) = 1$ where $\|X_t\| = X_t(D)$, cf. Def. 1.17, §1.15 of [14]. Next we are going to prove:

PROPOSITION 3. (Weak local extinction) *Let* $\mu(\neq 0)$ *be a finite measure with* supp$\mu \subset\subset D$. *Under the process* X_t *exhibits weak local extinction if and only if* $\lambda_c \leqslant 0$.

Proof. The fact that there exists a function $u > 0$ satisfying $(L+\theta)u = 0$ on $D(= \mathbb{G}^d)$ is equivalent to $\lambda_c \leqslant 0$. On the other hand, it is shown [15] that local extinction is also in fact equivalent to weak local extinction for superprocesses. Taking the positivity of the parameter $\beta > 0$ into consideration, the discussion in the proof of Theorem 2 finishes the proof of Proposition 3. □

Remark 1. A similar statement as Theorem 2 under a slightly different setup can be found in Lemma 4, §1.3 of [13].

Remark 2. A completely different proof of Proposition 3 can be found in §3 of 15], which is technically based upon Girsanov change of measure and change of measure for spatial branching processes.

Remark 3. When we assume that the DW superprocess X_t exhibits local extinction, if there exists a function $h \in C^{2,\varepsilon}$, $(0 < \varepsilon < 1)$ and a non-empty open ball $B \subset \mathbb{R}^d$ $(\neq \emptyset)$ such that $\inf_x \alpha h > 0$ and $(L+\theta)h \leqslant 0$ on $\mathbb{R}^d \setminus \bar{B}$, then X_t becomes extinct. A similar result have been proved under a different setup in [13], by using the h-transform technique for superdiffusions.

11 Concluding remarks

The result stated in Theorem 1 is known [1]. Our proof is due to variational derivative formalism for the generator of superprocess and is rather new, because they do not use the variational derivative approach in [1]. By virtue of the variational derivative approach, it is easy to get a better prospect for proving the convergence result. Hence, a new limit theorem for $X^{\gamma(x)}$ with spatially dependent branching rate can be derived as well.

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