

## Finite Time Extinction of Stochastic Model for Tumour Immunity

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腫瘍免疫確率モデルの有限時間消滅性  
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We are eager about a construction of mathematical immune models that describe the host-defense mechanism against cancer and also provide with a future useful and supplementary mathematical tool for medical treatment from a viewpoint of mathematical medicine. As is well known, there are two distinct models for tumour immune: one is a deterministic model and the other is a random model. In this article, based upon the probabilistic modelling method we propose an immune response model against cancer as a mathematical model of branching particle system. The peculiar features of this research consist in (i) proposing a special class of superprocesses as its limit; (ii) grasping the effects of immunity as the reflex extinction of the superprocess. Mathematically, the superprocess may arise from a system of branching particles by the renormalizing procedure, namely, by taking the short time high density limit of the system. The local extinction property of the model is extremely important on an applicational basis, because it just corresponds to the situation that the cancer cells are expelled locally by the actions of immune effectors. In this article we introduce our third model and in particular discuss the extinction of the model.

われわれはガンに対する生体防御機構を記述でき、数理医学的観点から将来治療に役に立つ補助的な数理道具を提供することにもつながる免疫モデルを数学的に構築することに意欲的に取り組んでいる。よく知られているように、腫瘍免疫に対しては2つの異なるモデルが存在している。1つは確定的モデルであり、いま1つはランダムなモデルである。本論文では確率論的なモデリング手法に基づいて、ガン細胞に対する免疫応答モデルを分枝粒子系の数理モデルとして提案する。本研究の特徴的な点は (i) 極限としての超過程の特別なクラスを取り扱うこと、(ii) その超過程の消滅性の現象的反映として免疫反応の効果をとらえることにある。数学的に見れば、超過程は再正規化手続きを取ることによって分枝粒子系から出現する。実際、その手続きは世代交代の時間間隔を短縮し個体質量を矮小化する高密度化極限を取ることによって実現されるものである。モデルの局所消滅という性質は、ガン細胞が免疫作用によって局所的に駆逐される様子に対応すると考えられるので応用上極めて重要である。この論文では第3モデルを紹介し、そのモデルの消滅性について議論する。

## 1 Introduction

The purpose of this research consists in modelling mathematically the immune response against cancer cells. Ordinarily, some of normal cells are transformed into irregular ones by several reasons, such as chemicals, carcinogens, carcinogenic virus and bacteria, DNA replication error, DNA repair disorder, chromosomal end centromere disorder, radiation and so on, and the tumorigenic process proceeds. In concord with that, a group of immune cells invoke the immune response against canceration, and in so

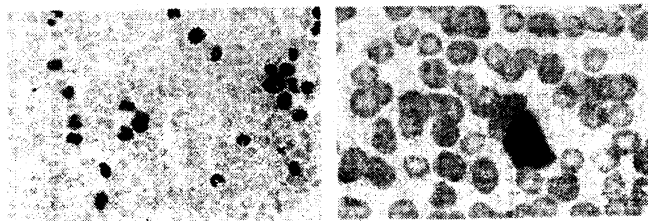


図 1: cancer cells (pa.1)

doing they accomplish their important errand of host-defense mechanism in the living body. Here the

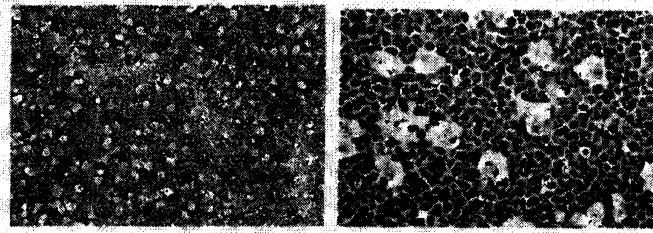


図 2: cancer cells (pa.2)

effectors are supposed to be NK (naturak killer) cells, cytotoxic T cells, and activated macrophages, etc. We focus our mind especially on the immune response both in the transformation period of cell and in the proliferation period of cancerated cell, and propose a stochastic model that is capable to describe the cytotoxic actions by a bunch of effectors against cancer cells. Analyzing the model mathematically, we study the qualitative properties of the biological phenomena related to immune response against cancer. In our previous research [6] for our first primitive model we introduced the immigration rate  $q > 0$  (a positive constant) as the cytotoxic intensity of effectors against cancer. In the succeeding paper [9] we improve this point and propose a more elaborate model that can describe the effects by those effectors, depending on the location in accordance with the environmental changes. In this article as our third model we introduce a new model that allows the effector field to change itself depending on the associated environmental change. In this paper we may adopt stochastic modelling approach [13] to grasp the immune response against cancer as a mathematical model of branching particle system, and to consider the effectiveness of immunity as a reflection of extinction property on superprocesses. In [1] we considered a formulation of catalytic processes applicable to filaments and catalysts in physiology and biochemistry, and studied asymptotic behaviours of solutions to related equations. While, in [2] we investigated a special class of stochastic processes related to chemical reaction of the medicinal, and proved the existence and uniqueness theorem for measure-valued processes which is able to describe the increase or decrease of a branching particle system in number according to whether the environment is good or not.

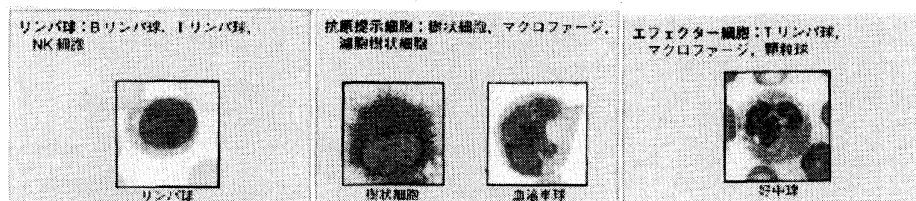
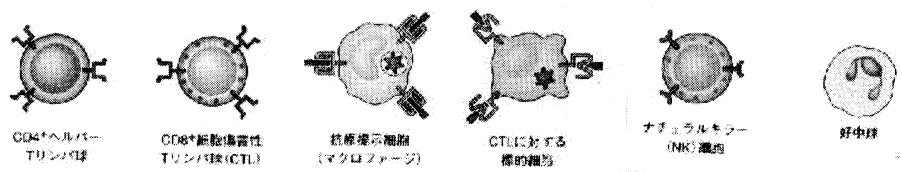
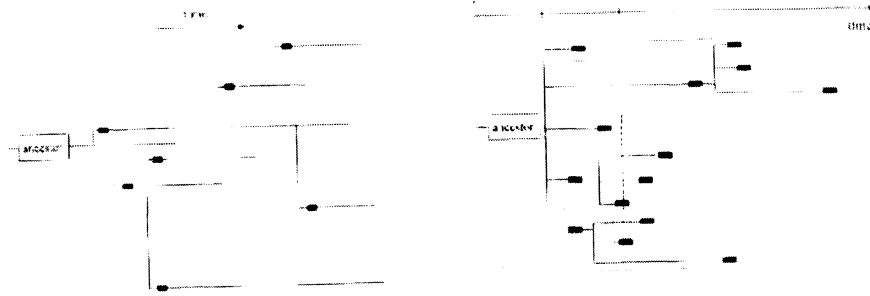


図 3: the immune cells: effectors (pa.3)



## 2 Stochastic model for immune response against cancer

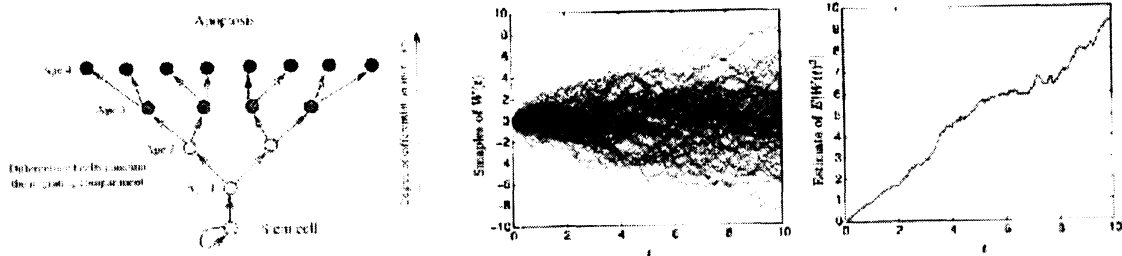
The immune system in the living body is regulated by the effector-induction protocol. It is known that various kind of effectors (such as T cells, B cells, NK cells, NKT cells, dendritic cells, and macrophages, etc.) form a very complicated network, and that there is a possibility that it provokes a positive and/or negative immune response for/against cancer cells. Our main concern is antitumor immune response, and NK cells, NKT cells and T cells have to do with the immune surveillance for cancerated cells. When the tumorigenic process proceeds, normal cells are transformed into irregular ones by some reasons and are



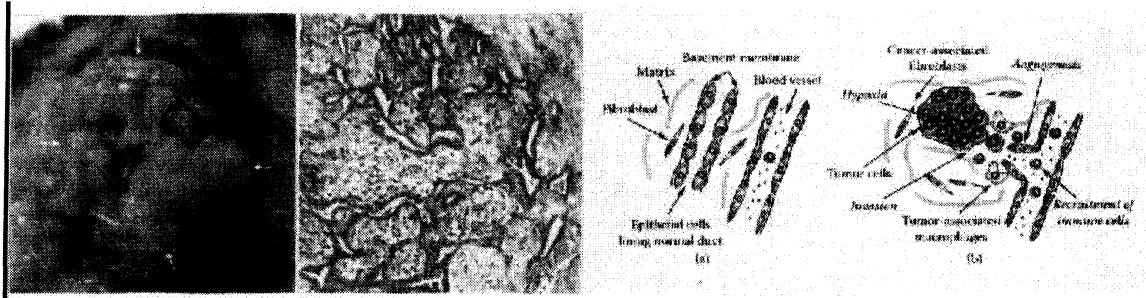
cancerated, and they repeat disorder proliferation peculiar to the cancer because of continual emission of false proliferation signals by malfunctioned oncogenes and tumor suppressor genes. On the other hand, the cancer cell is preyed or destroyed by effectors (a group of immune cells such as NK cells and so on) by virtue of the immune surveillance mechanism in a living body. Then, taking them all into consideration, we introduce a natural number valued random variable  $N_n : \Omega \rightarrow N$  for each  $n$ , which means the total number of cancer cells in the  $n$ -th generation. We assume that there is a sequence  $\{\gamma_n\}_n$  of positive numbers such that  $\gamma_n \rightarrow \gamma \in \mathbb{R}^+$  (as  $n \rightarrow \infty$ ) and also that

$$\mathbb{E}[\xi_n] = 1 + \frac{\gamma_n}{n}, \quad \text{Var}(\gamma_n) = \sigma_n^2 \rightarrow \sigma^2 \quad (\text{as } n \rightarrow \infty) \quad (1)$$

where  $\gamma_n$  is the number of offsprings generated by the  $n$ -th generation. This implies that the branching particle system has a clear tendency to increase in number. When we suppose that for each cell, the proliferation or division occurs independently at a random time, we introduce the branching rate  $n\lambda$  ( $\lambda > 0$ ), which means the accelerated increase rate for the number of cancer cells. We adopt a model by a branching particle system as a proliferation process for cancer. The second expression in (1) implies that the finiteness of the varinace (or the second moment) will be kept even in the passage to the limit  $n \rightarrow \infty$ .



Since we have only to describe the immune response in a locally limited tissue, the region in question is restricted to a comparatively small area. So that, it suffices to consider the model in a bounded domain  $D \subset \mathbb{R}^d$  with  $d = 3$ . For  $N_n$  pieces of cancer cells in the  $n$ -th generation, each cancer cell is supposed to start at the initial point  $x_i^{(n)} \in \mathbb{R}^d$  ( $i = 1, 2, \dots, N_n$ ). While, it is considered that the target cell (= the cancer cell) moves little in the early stage, namely in the transformation period of cell, and also that in the proliferation period of cancerated cell it may diffuse and expand as if the liquid should seep through a leather bag because of a superfluity of proliferated cancer cells. Hence, we regard it as a diffusion with diffusion coefficient  $k(\varepsilon)$  depending on a small parameter  $\varepsilon (> 0)$ . The diffusion operator is defined as  $L_\varepsilon = k(\varepsilon)\Delta$ , where  $\Delta$  is the Laplacian.



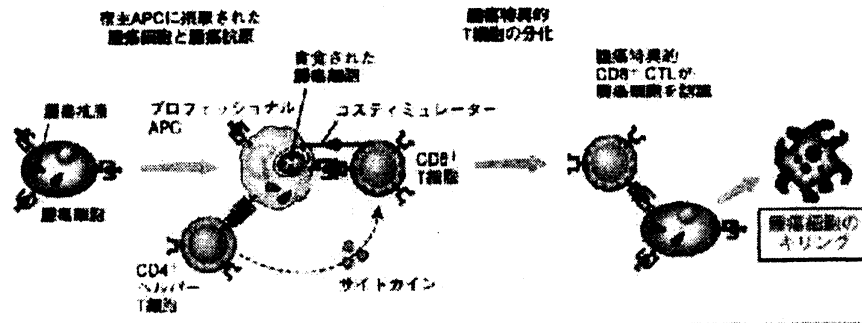
In our model the effectors are supposed to be NK cells, killer T cells, macrophages among a group of immune cells, and we will take the cytotoxicity of these effectors against cancer into account. In the previous paper [6], the previous report [4] or the previous announcements [3] (see also [5]), we introduce a deterministic emigration rate  $q > 0$  (a positive constant) in the terminology of the theory of stochastic processes, which expresses the intensity of cytotoxicity by effectors against cancer. Although one may find it interesting as the first random model, it is not necessarily desirable to treat it like a simple and poor model, in order to imitate the effects of immune response by effectors against cancer from the viewpoint of the modelling theory as well as from the standpoint of future simulation analysis. In the succeeding studies [9] we improve this point and propose a more elaborate model, which can describe the effects by those effectors, depending on the location in accordance with the environment changes. There are three methods in the improvement. That is, it means that instead of the positive constant  $q$ , we adopt a (random) function  $q$  like:

$$(i) q(x), \quad x \in D; \quad (ii) q(\omega) \quad \text{or} \quad q(\omega, x), \quad \omega \in \Omega; \quad (iii) q(t, \omega), \quad \omega \in \Omega.$$

In the model (i) the intensity of cytotoxicity  $q$  depends on the location  $x \in D$ , which means that the intensity  $q(x)$  varies as the environment changes, and it strengthens or weakens according to the good or bad environment. In the second new model the parameter  $\omega$  expresses the environmental change independent of the sample  $\omega'$  which comes from the original stochasticity of the branching model. The latter case  $q(\omega, x)$  just corresponds to the case  $q(\omega)$  depending on the location. In the model (iii) the time evolution of  $q(\omega)$  can also be described. As a matter of fact, we can realize the case (i) as the choice of branching rate  $\alpha(x)$  and branching mechanism  $\beta(x)$  depending on the location, for example. The aim of this article is to establish the realization of the case (ii) through a construction of catalytic process which belongs to a special class of superprocesses. Once it has been accomplished, the next target should be a derivation of extinction property of the model. Under the above-mentioned settings, we propose a random model for the target cancer cells:

$$X_t^{(n)} = \frac{1}{n} \sum_{i=1}^{N_n(t)} \delta_{x_i^{(n)}(t)} \quad (2)$$

where  $x_i^{(n)}(t)$  is the location of the  $i$ -th cancer cell in the  $n$ -th generation at time  $t$ , and  $N_n(t)$  denotes the total number of cancer cells alive at time  $t$ . (2) is the quantity related to an empirical measure, expressing the state of the cancer at time  $t$ . For instance, the qualitative property of a random walk is well reflected by its limiting process, say, the Brownian motion. Likewise, the qualitative property of an aggregate of cancer cells can be thought to be reflected by its limiting process  $X_t$ . On this account, we have to only to analyze the limit superprocess  $X_t$  in what follows.



### 3 Analysis on the limiting process

Let  $C = C(\mathbb{R}^d)$  be the space of continuous functions on  $\mathbb{R}^d$ . When  $C_b$  denotes the set of bounded continuous functions on  $\mathbb{R}^d$ , then  $C_b^+$  is the set of positive members  $g$  in  $C_b$ . Let  $\langle \mu, f \rangle = \int f d\mu$ , and  $M_F = M_F(\mathbb{R}^d)$  is the space of finite measures on  $\mathbb{R}^d$ . We denote an  $L_\varepsilon$ -diffusion process by  $\Xi = \{\xi, \Pi_{s,a}, s \geq 0, a \in \mathbb{R}^d\}$ . Then  $K \equiv K(dr)$  is the associated continuous additive functional (CAF), and we assume that  $K$  lies in the Dynkin locally admissible class [10] of CAF, and we write it as  $K \in \mathbb{K}^q$  (some  $q > 0$ ). Then a superprocess  $\mathbb{X} = \{X, \mathbb{P}_{s,\mu}, s \geq 0, \mu \in M_F\}$  with branching rate functional  $K$  (or  $(L_\varepsilon, K, \mu)$ -superprocess) can be characterized as a continuous  $M_F$ -valued time-inhomogeneous Markov process  $X = \{X_t\}$  with Laplace functional

$$\mathbb{P}_{s,\mu} e^{-\langle X_t, \varphi \rangle} = e^{-\langle \mu, v(s,t) \rangle}, \quad 0 \leq s \leq t, \quad \mu \in M_F, \quad \varphi \in C_b^+. \quad (3)$$

Here the function  $v$  is uniquely determined by the log-Laplace equation

$$\Pi_{s,a} \varphi(\xi_t) = v(s,a) + \Pi_{s,a} \int_s^t v^2(r, \xi_r) K(dr), \quad 0 \leq s \leq t, \quad a \in \mathbb{R}^d. \quad (4)$$

We need Dynkin's Historical Superprocess.  $\mathbb{C} = C(\mathbb{R}_+, \mathbb{R}^d)$  denotes the space of continuous paths on  $\mathbb{R}^d$  with topology of uniform convergence on compact subsets of  $\mathbb{R}_+$ . To each  $w \in \mathbb{C}$  and  $t > 0$ ,  $w^t \in \mathbb{C}$  expresses the stopped path of  $w$ , and  $\mathbb{C}^t$  is the totality of all these paths stopped at time  $t$ . To every  $w \in \mathbb{C}$ , putting  $\tilde{w}_t = w^t$ ,  $t \geq 0$ , we associate the corresponding stopped path trajectory  $\tilde{w}$ . The image of  $L_\varepsilon$ -diffusion  $w$  under the map  $w \rightarrow \tilde{w}$  is called the  $L_\varepsilon$ -diffusion path process. We define  $\mathbb{C}_R^\times \equiv \mathbb{R}_+ \hat{\times} \mathbb{C} = \{(s, w) : s \in \mathbb{R}_+, w \in \mathbb{C}^s\}$ . We consider the set  $M(\mathbb{C}_R^\times) \equiv M(\mathbb{R}_+ \hat{\times} \mathbb{C})$  of measures  $\gamma$  on  $\mathbb{R}_+ \hat{\times} \mathbb{C}$  which are finite, if restricted to a finite time interval. Then Dynkin's historical superprocess [10]

$$\tilde{\mathbb{X}} = \{\tilde{X}, \tilde{\mathbb{P}}_{s,\mu}, s \geq 0, \mu \in M_F(\mathbb{C}^s)\}$$

is defined as a time-inhomogeneous Markov process with state  $\tilde{X}_t \in M_F(\mathbb{C}^t)$ ,  $t \geq s$ , with Laplace functional

$$\langle \mu, v(s,t) \rangle = -\log \tilde{\mathbb{P}}_{s,\mu} e^{-\langle \tilde{X}_t, \varphi \rangle}, \quad 0 \leq s \leq t, \quad \mu \in M_F(\mathbb{C}^s), \quad \varphi \in C_b^+(\mathbb{C}) \quad (5)$$

where  $v$  is uniquely determined by the log-Laplace type equation

$$\tilde{\Pi}_{s,w_s}\varphi(\tilde{\xi}_t) = v(s, w_s) + \tilde{\Pi}_{s,w_s} \int_s^t v^2(r, \tilde{\xi}_r) \tilde{K}(dr), \quad 0 \leq s \leq t, \quad \mu \in M_F(\mathbb{C}^s), \quad \varphi \in C_b^+(\mathbb{C}). \quad (6)$$

**THEOREM 1.** *Let  $K \in \mathbb{K}^n$  and  $\mu \in M_F$  with compact support. Then there exists an  $(L_\varepsilon, K, \mu)$ -superprocess*

$$\mathbb{X} = \{X, \mathbb{P}_{s,\mu}, s \geq 0, \mu \in M_F\}$$

with branching rate functional  $K$ .

**THEOREM 2.** *There exists a Dynkin's historical superprocess  $\tilde{\mathbb{X}} = \{\tilde{X}, \tilde{\mathbb{P}}_{s,\mu}, s \geq 0, \mu \in M_F(\mathbb{C}^s)\}$ .*

Suppose that  $p > d$ , and let  $\phi_p(x) = (1 + |x|^2)^{-p/2}$  be the reference function. Define  $C_p = \{f \in \mathbb{C} : |f| \leq C_f \cdot \phi_p, \exists C_f > 0\}$ . We denote by  $M_p = M_p(\mathbb{R}^d)$  the set of non-negative measures  $\mu$  on  $\mathbb{R}^d$ , satisfying  $\langle \mu, \phi_p \rangle = \int \phi_p(x) \mu(dx) < \infty$ . It is called the space of  $p$ -tempered measures. When  $\{\xi_t, \Pi_{s,a}\}$  is an  $L_\varepsilon$ -diffusion, then we define the continuous additive functional  $K_\eta$  of  $\xi$  by

$$K_\eta = \langle \eta, \delta_x(\xi_r) \rangle dr = \left( \int \delta_X(\xi_r) \eta(dx) \right) dr \quad \text{for } \eta \in M_p. \quad (7)$$

Then  $X^\eta = \{X_t^\eta; t \geq 0\}$  is nothing but a measure-valued diffusion with branching rate functional  $K_\eta$ . Next we assume that  $d = 1$  and  $0 < \nu < 1$ . Let  $\lambda \equiv \lambda(dx)$  be the Lebesgue measure on  $\mathbb{R}$ , and let  $(\gamma, \mathbb{P})$  be the stable random measure on  $\mathbb{R}$  with Laplace functional

$$\mathbb{P}e^{-(\gamma, \varphi)} = \exp \left\{ - \int \varphi^\nu(x) \lambda(dx) \right\}, \quad \varphi \in C_b^+. \quad (8)$$

Note that  $\mathbb{P}$ -a.a  $\omega$  realization,  $\gamma(\omega) \in M_p$  under the condition  $p > \nu^{-1}$ . We consider a positive CAF  $K_\gamma$  of  $\xi$  for  $\mathbb{P}$ -a.a.  $\omega$ . So that, thanks to Dynkin's general formalism for superprocess with branching rate functional, there exists an  $(L_\varepsilon, K_\gamma, \mu)$ -superprocess  $X^\gamma$  when we adopt a  $p$ -tempered measure  $\gamma$  for CAF  $K_\eta$  in (7) instead of  $\eta$ , as far as  $K_\gamma = K_\gamma(\omega; dr)$  may lie in the class  $\mathbb{K}^q$  for some  $q > 0$ .

**THEOREM 3.** *Let  $K_\gamma \in \mathbb{K}^q$ . For  $\mu \in M_F$  with compact support, there exists an  $(L_\varepsilon, K_\gamma, \mu)$ -superprocess  $\{X^\gamma, \mathbb{P}_{s,\mu}^\gamma, s \geq 0\}$  with branching rate functional  $K_\gamma$ .*

**EXAMPLE 4.** For  $d = 1, a = 1$  and  $b = 0$ ,  $X^\gamma$  is a stable catalytic SBM. This was initially constructed and investigated by Dawson-Fleischmann-Mueller (2000).

Since the initial measure  $\mu$  has compact support, according to Dawson-Li-Mueller (1995),  $X^\gamma$  has the compact support property, with the result that the range  $\mathfrak{R}(X)$  of  $X^\gamma$  is compact. We are going to work with historical superprocesses. As a matter of fact, for the sake of convenient criterion, we put the superprocess  $X^\gamma$  lifted up to the historical superprocess setting  $\tilde{X}_t^\gamma(dw)$ . For a path  $w \in \mathbb{C}$ , we consider the stopped path  $w^t \in \mathbb{C}$  defined by  $w_s^t = w_{t \wedge s}$ , ( $s \geq 0$ ). Then we can show the existence of the corresponding historical superprocess in the Dynkin sense.

**THEOREM 5.** *Let  $K_\gamma$  be a positive CAF of  $\xi$  lying in the Dynkin class  $\mathbb{K}^q$ . Then there exists a historical superprocess  $\{\tilde{X}^\gamma, \tilde{\mathbb{P}}_{s,\mu}^\gamma, s \geq 0\}$  in the Dynkin sense. In fact,  $\tilde{\mathbb{X}}^\gamma = \{\tilde{X}^\gamma, \tilde{\mathbb{P}}_{s,\mu}^\gamma, s \geq 0, \mu \in M_F(\mathbb{C}^s)\}$  is a time-inhomogeneous Markov process with state  $\tilde{X}_t^\gamma \in M_F(\mathbb{C}^t)$ ,  $t \geq s$ , with Laplace transition functional*

$$\tilde{\mathbb{P}}_{s,\mu}^\gamma \exp \left\{ - \langle \tilde{X}_t^\gamma, \varphi \rangle \right\} = e^{-\langle \mu, v(s,t) \rangle}, \quad 0 \leq s \leq t, \mu \in M_F(\mathbb{C}^s), \varphi \in C_b^+(\mathbb{C}), \quad (9)$$

where the function  $v$  is uniquely determined by the log-Laplace type equation

$$\tilde{\Pi}_{s,w_s}\varphi(\tilde{\xi}_t) = v(s, w_s) + \tilde{\Pi}_{s,w_s} \int_s^t v^2(r, \tilde{\xi}_r) \tilde{K}_\gamma(\omega; dr), \quad 0 \leq s \leq t, \quad w_s \in \mathbb{C}^s. \quad (10)$$

Roughly speaking, in order to prove our result Theorem 5, we need to apply Theorem 3 to historical process. We shall adopt some notation and terminology from Dynkin (1991). Let  $(E_t, \mathcal{B}_t)$  be a measurable space that describes the state space of the underlying process  $\xi$  at time  $t$  (which can usually be imbedded isomorphically into a compact metrizable space  $C$ ), and  $\hat{E}$  be the global state space given by the set of pairs  $t \in \mathbb{R}_+$  and  $x \in E_t$ . The symbol  $\mathcal{B}(\hat{E})$  denotes the  $\sigma$ -algebra in  $\hat{E}$ , generated by functions  $f : \hat{E} \rightarrow \mathbb{R}$ . Note that  $\hat{E}(I) = \{(r, x) : r \in I, x \in E_r\} \in \mathcal{B}(\hat{E})$  for every interval  $I$ . The sample space  $W$  is a set of paths (or trajectories)  $\xi_t(w) = w_t$  for each  $w \in W$ . Furthermore,  $\mathcal{F}(I)$  is the  $\sigma$ -algebra generated by  $\xi_t(w)$  for  $t \in I$ . Let  $w(I)$  denote the restriction of  $w \in W$  to  $I$ , and  $W(I)$  be the image of  $W$  under this mapping. Moreover,  $\tilde{\Xi} = (\xi_{\leq t}, \mathcal{F}_{\tilde{\Xi}}(I), \tilde{\Pi}_{r, w(\leq r)}) = (\xi(-\infty, t], \mathcal{F}_{\tilde{\Xi}}(I), \tilde{\Pi}_{r, w(-\infty, r]})$  is the historical process for  $\xi = (\xi_t, \mathcal{F}(I), \Pi_{r, a})$ . Under those circumstances, it suffices to prove the following assertion in order to prove the main result Theorem 5.

**THEOREM 6.** *Let  $\tilde{\Xi}$  be a historical process,  $\tilde{K}_\gamma = \tilde{K}_\gamma(w)$  be its CAF associated to stable random measure  $\gamma$  with properties:*

(a) *For every  $q > 0$ ,  $r < t$  and  $x \in E_r$ ,  $\tilde{\Pi}_{r, x(\leq r)} e^{q\tilde{K}_\gamma(w; (r, t))} < \infty$ . (b) *For every  $t_0 < t$ , there exists a positive constant  $C$  such that  $\tilde{\Pi}_{r, x(\leq r)} \tilde{K}_\gamma(w; (r, t)) \leq C$  holds for  $r \in [t_0, t)$ ,  $x \in E_r$ . Put  $\psi^t(x, z) = b^t(x)z^2 = 1 \times z^2$ . Then there exists a Markov process  $M^\gamma = (M_t^\gamma, \mathcal{G}(I), P_{r, \mu}^\gamma)$  on the space  $\mathcal{M}_{\leq t} = M_F(\mathbb{C}^t)$  of all finite measures on  $(W, \mathcal{F}_{\leq t}^*) = (W, \mathcal{F}^*(-\infty, t])$  with the universal completion  $\mathcal{F}_{\leq t}^*$  of  $\sigma$ -algebra, such that for every  $t \in \mathbb{R}_+$  and  $\varphi \in \mathcal{F}_{\leq t}^*$ ,**

$$P_{r, \mu}^\gamma \exp \{-\langle M_t^\gamma, \varphi \rangle\} = e^{-\langle \mu, v(r, \cdot) \rangle}, \quad 0 \leq r \leq t, \quad \mu \in \mathcal{M}_{\leq r}, \quad (11)$$

where  $v^r(w_{\leq r}) = v(r, w(-\infty, r])$  is a progressive function determined uniquely by the equations

$$\begin{aligned} v^r(x_{\leq r}) + \tilde{\Pi}_{r, x(\leq r)} \int_r^t \psi^s(\xi_{\leq s}, v^s(\xi_{\leq s})) \tilde{K}_\gamma(w; ds) &= \tilde{\Pi}_{r, x(\leq r)} \varphi(\xi_{\leq t}) \quad \text{for } r \leq t \\ v^r(x_{\leq r}) &= 0 \quad \text{for } r > t. \end{aligned} \quad (12)$$

Let  $\mathbb{H}$  be the cone of all bounded functions  $f \in \mathcal{B}$  with the topology of bounded convergence. In addition, we define  $\mathbb{H}_c = \mathbb{H} \cap \{f : 0 \leq f \leq c\}$ . In order to prove Theorem 3 we need the following lemma. Based upon the discussion on approximation in terms of branching particle systems cf. Dynkin (1994), we suppose that the function  $v_t^r(\beta, x)$  satisfies

$$v_t^r(\beta, x) + \Pi_{r, x} \int_r^t \psi_\beta^s(\xi_s, v_t^s(\beta, \xi_s)) K_\gamma(w; ds) = \Pi_{r, x} F_\beta(\xi_t) \quad (13)$$

with  $F_\beta(x) = \frac{1}{\beta}(1 - e^{-\beta f(x)})$ .

**LEMMA 7. (Key Lemma)** *Let  $K_\gamma$  be the CAF of  $\xi$ . For  $\beta > 0$ , we assume that  $\psi_\beta^t(x, z)$  converges to  $\psi^t(x, z)$  uniformly on the set  $(t, x) \in \hat{E}$ ,  $z \in [0, c]$  for every  $c \in (0, \infty)$ . Then the function  $v_t^r(\beta, x)$  given by (13) converges uniformly on every set  $r \in [t_0, t)$  and  $f \in \mathbb{H}_c$  to the unique solution  $v^r(x)$  of the following integral equation*

$$\begin{aligned} v^r(x) + \Pi_{r, x} \int_r^t \psi^s(\xi_s, v^s(\xi_s)) K_\gamma(w; ds) &= \Pi_{r, x} f(\xi_t) \quad \text{for } r \leq t \\ v^r(x) &= 0 \quad \text{for } r > t. \end{aligned} \quad (14)$$

In the previous work [6] (see also [3–5]) we have recognized that the extinction property of super-processes is very important in the model argument. Especially as far as local extinction is concerned, it is of extreme interest and importance because it just corresponds to the situation that the cancer cells are expelled locally from the cancerated area by the immune effects of effectors. Since the initial measure  $\mu \in M_F$  has a compact support, it follows from the argument of compact support property

that the range  $\mathfrak{R}(X)$  of  $X$  is compact. Under the historical superprocess setting  $\tilde{X}_t(dw)$ , we define  $\mathbb{C}_M = \{w \in \mathbb{C} : |w_s| < M, \forall s \geq 0\}$  for  $M \geq 1$ . By the compact support property, we have

$$\lim_{K \rightarrow \infty} \inf_{t \geq 0} \tilde{\mathbb{P}}_{0,\mu} \left( \text{supp}(\tilde{X}_t) \subseteq \mathbb{C}_M \right) = 1, \quad \mathbb{P} - \text{a.a.}\omega.$$

PROPOSITION 8. For  $K \in \mathbb{K}_\eta$ ,  $\lim_{t \rightarrow \infty} \tilde{\mathbb{P}}_{0,\mu}(\tilde{X}_t \neq 0)$ , and  $\text{supp}(\tilde{X}_t) \subseteq \mathbb{C}_M = 0$ .

Finally, through the projection technique in the theory of measure-valued processes we obtain

THEOREM 9. (**Extinction property**) Let  $d = 1$  and  $\mu \in M_F$  with compact support. Then

$$\mathbb{P}_{0,\mu}(X_t = 0 \text{ for some } t > 0) = 1.$$

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