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A STOCHASTIC MODEL OF THE TUMOR GROWTH FOR ADJUVANT CHEMOTHERAPY OF CANCER

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ABSTRACT

A stochastic model is developed to describe the growth of a heterogeneous tumor for adjuvant chemotherapy. The mathematical model is a quasilinear stochastic partial differential equation driven by a space-time white noise. The main feature of the model is that it takes into account random independent interactions between tumor cells, effector cells and anticancer drugs. The paper is primarily focused on the proofs of the existence, comparison theorem and the uniqueness in law of weak solutions to the martingale problem associated with the model.

PËRMBLEDHJE

Ndërtohet një model stokastik që përshkruan rritjen e një tumori heterogjen per kimioterapinë ndihmëse. Modeli stokastik është një ekuacion kuazilinear me derivate të pjesshme i drejtuar nga një zhurmë e bardhë në hapësirë-kohë.Veçoria kryesore e modelit është se ai merr parasysh bashkëveprimet e pavarura të rastit ndërmjet qelizave tumorale, qelizave të sistemit imunitar dhe ilaçeve anticancerozë. Studimi ynë është përqëndruar kryesisht në vërtetimet e ekzistencës së zgjidhjes, teoremës së krahasimit dhe unicitetit në kuptimin e ligjit të shpërndarjes të zgjidhjeve të dobta të problemit martingal shoqërues të modelit të shqyrtuar.

Key words: Tumor growth, stochastic partial differential equation, white noise, weak existence, uniqueness in law.

INTRODUCTION

Cancer is a multi-step process consequent on the breakdown of normal cellular interactions and control of replication. We recognize that each cancer corresponds to a particular genetic pathway and that the behavior of cancer cells is characterized by:

- an autonomous and unrestrained growth,
- an ability to escape immune surveillance,
- an invasion into the surrounding tissue,
- a metastatic potential,
- an acquired or induced resistance to the drugs [6,9,10,12].

All these features of cancer cell behavior can be explained in terms of genetic changes and the functional impact of these changes. Mathematical models of the tumor growth have been traditionally developed in the framework of continuum mechanics, which is based upon the diffusion equation involving moving boundary effect, but without taking into account tumor – host cell interactions. This topic is dealt with by several authors. A new methodological approach, based on cellular kinetic theory was developed in [2] for modeling on the interactions between tumor cells and immune system cells. Stochastic models of the tumor growth driven by a Wiener process have been investigated in many cases [6, 13].

After reviewing a great amount of publications concerning stochastic modeling of tumor growth, we conclude that the proposed model is probably the first model of tumor growth by stochastic partial differential equations, driven by a space-time white noise. Resistance to chemotherapy represents a well-organized barrier to the effective treatment of cancer patients. Resistance to adjuvant chemotherapy depends on the presence of drug resistant tumor cells. Recurrent cancer and metastatic disease often results from the outgrowth of tumor cells that are resistant to chemotherapy [6, 10]. Resistance to anticancer drug is a combined characteristic of a specific drug, a specific tumor and specific host. The modeling of drug resistance is not without some controversy. Coldman

and Goldie [3] state that "the sensitive tumor cells have a constant probability for division of acquired resistance to a particular drug to a particular dose", but Rosen [19] believes that drug resistance is independent on dose. We agree with Coldman and Goldie. The present paper deals with the development of a quasilinear stochastic model of tumor growth in the presence of adjuvant chemotherapy. The paper is organized in three sections. After this introduction, Section 2 deals with the development of the mathematical model. Section 3 deals with the existence of weak solutions and uniqueness in law. In a forthcoming paper we will study with probabilistic methods several applications of Theorem 3.1 and Theorem 3.3 in adjuvant chemotherapy of cancer.

MODEL

The biological system we want to study is constituted, at the cellular level, of the following three main populations:

- Tumor cells, characterized by an anomalous proliferation and the difficulty to receive inhibitory and apoptotic signals.
- Environment cells, characterized by promoting (feeding) influence over tumor cells.
- Immune cells potentially able to either strongly hamper or favor tumor growth.

We proceed from the following biomedical assumptions:

B_1 - All tumor cells behave independently of each other [10].

B_2 - The lytic rate of tumor cells due to destructive action of effector cells is Michaelian or Lefeverian or Kuznetsovian [14-15]

B_3 - The tumor will consist of drug sensitive and drug resistant cells.

B_4 - All progeny of resistant tumor cells are assumed to be resistant.

B_5 - The drug resistance develops during treatment, due to the presence of the drug.

$\mathbf{B_6}$ - No sensitive tumor cell becomes resistant during its lifetime.

B_7 - There is no drug building up in the host environment.

B_8 - There is no accumulation of dead cells.

B_9 - The rate of sensitive tumor cell lost due to the drug will be considered proportional to an increasing function of the drug concentration within the tumor and an increasing function of the current sensitive tumor cells population size [4, 17].

Random independent interactions between tumor cells, effector cells and anticancer drugs suggest a modeling of the tumor growth based on stochastic partial differential equations 2.1 and 2.2:

$$\left.\begin{aligned}\frac{\partial u}{\partial t}&=D\frac{\partial^2 u}{\partial r^2}+\varphi(t,r,w,u)-l(t,r,w,u)-d(t,r,w,u)-\alpha\varphi(t,r,w,u)u\\&+G(t,r,w,u)\frac{\partial^2 W(t,r)}{\partial t\partial r}\qquad for\quad t\in R_+,\quad r\in[0;a],\quad w\in\Omega\end{aligned}\right\}$$

(2.1)

The initial and boundary conditions

$$u(0,r,w)=u_0(r,w)\qquad for\quad r\in[0;a],\quad w\in\Omega$$

$$u(t,0,w)=u(t,a,w)=0\quad for\quad t\in R_+,\quad w\in\Omega$$

$$\left.\begin{aligned}\frac{\partial v}{\partial t}&=D_1\frac{\partial^2 v}{\partial r^2}+\varphi_1(t,r,w,v)-l_1(t,r,w,v)-d(t,r,w,u)-\alpha\varphi(t,r,w,u)u\\&+G_1(t,r,w,u)\frac{\partial^2 W_1(t,r)}{\partial t\partial r}\qquad for\quad t\in R_+,\quad r\in[0;a],\quad w\in\Omega\end{aligned}\right\}$$

(2.2)

The initial and boundary conditions

$$v(0,r,w)=v_0(r,w)\qquad for\quad r\in[0;a],\quad w\in\Omega_1$$

$$v(t,0,w)=v(t,a,w)=0\qquad for\quad t\in R_+,\quad w\in\Omega_1$$

Les us explain the problems (2.1) and (2.2).

Let denote $\theta = (\Omega, F, F_t, P)$ as a filtered probability space carrying a set-valued white noise W (t, r) on $R_+ \times [0; a]$. This means W (t, r) is a random set function from $B(R_+ \times [0; a])$ into $L^2(\Omega,F,P)$ such that

1. $\forall A,B\in B(R_+\times[0;a])$ with $A\cap B=\Phi$ (empty set) the random variables $W(A)$ and $W(B)$ are independent, and $W(A\cup B)= W(A)+ W(B)$

2. $\forall C\in B([0;a])$ the random process $(W([0;t]\times C))_{t\geq 0}$ is an F_t-Brownian motion with covariance function $t\,L(c)$, where L denotes the Lebesgue measure and $B(H)$ denotes the Borel sets of topological space H.

Since $\frac{\partial^2 W(t,r)}{\partial t\partial r}$ is P-almost surely nowhere differentiable, the space-time white noise $\frac{\partial^2 W(t,r)}{\partial t\partial r}$ can only be defined in terms of the random Schwartz distributions [11, 20]. $u(t, r, w)$ represents the density number of drug sensitive tumor cells at time t and site r, the Fickian diffusion term is $D\frac{\partial^2 u}{\partial r^2}$ one-dimensional nearest neighbor migration due to cellular replication (more generally, this term included to model cellular motion), and $D\cong\lambda d^2$ where λ denotes the replication rate of tumor cells and d is the diameter of a tumor cell.

In the equations above, $\varphi(u)$ represents the proliferative rate of drug sensitive tumor cells, $l(u)$

represents the lytic rate of drug sensitive tumor cells due to destructive action of effector cells, $d(u)$ represents the rate of drug sensitive tumor cells lost to anticancer drug, $\alpha=\alpha(t,r,w)$ represents the mutation rate from sensitive to resistant tumor cells according to Coldman-Goldie model (i.e. α is the fraction per unit of time of the drug sensitive tumor cells that mutates into drug resistant cells), GW represents the driving noise term for random independent interactions between drug sensitive tumor cells, effector cells and drugs, $v=(t,r,w)$ represents the density number of drug resistant tumor cells, $\varphi_1(v)$ represents the proliferative rate of drug resistant tumor cells, G_1W_1 represents the driving noise term for random independent interactions between drug resistant tumor cells, effector cells and drugs, u_0 and v_0 represent the initial density number of drug sensitive and drug resistant tumor cells.

Under the assumption B_1 the variance of tumor cells subpopulation variation is proportional to the tumor cells density number.

$$G(t,r,w,u)\cong\sqrt{u}\ ,\text{ and }\ G_1(t,r,w,v)\cong\sqrt{v}$$

Hence, b and b_1 are not Lipschitz near zero. Assuming that,

$$G(t,r,w,u)=\sqrt{B(t,r,w)u} \qquad \text{or}$$

$$G(t,r,w,u)=\sqrt{B(t,r,w)u(b-u)}$$

Where $B(t,r,w)$ is the branching rate of sensitive tumor cells at time t and site r.

The following changes of variable:

$t\to\lambda t,\ \ r\to\sqrt{\frac{\lambda}{D}}\cdot r$, (where λ is the mean value of the rate for the cellular replication of the drug sensitive tumor cells) reduces (2.1) to dimensionless equation:

$$\left.\begin{aligned}\frac{\partial u}{\partial t}=D\frac{\partial^2 u}{\partial r^2}+f(t,r,w,u)+g(t,r,w,u)\frac{\partial^2 W(t,r)}{\partial t\partial r}\\ for\quad t\in R_+,\quad r\in[0;a],\quad w\in\Omega\end{aligned}\right\}$$

(2.3)

Where, $f=\frac{\phi-l-d-\alpha\phi u}{\lambda}$, $g=\frac{cG}{\lambda}$, $a\to\sqrt{\frac{\lambda}{D}}\cdot a$ and $\frac{\partial^2 W(t,r)}{\partial t\partial r}$ is another space-time white noise. We observe that if $W(t, r)$ is a set-indexed white noise, and then $\sqrt{ab}W(at,br)$ is also a set-indexed white noise, $\forall a,b>0$ constants. The SPDE (2.3) describes a continuum limit in space of one-dimensional model of the tumor growth for dispersed cells regime. Similarly, we find

$$\left.\begin{aligned}\frac{\partial v}{\partial t}=D_1\frac{\partial^2 u}{\partial r^2}+f_1(t,r,w,v,u)+g_1(t,r,w,v,u)\frac{\partial^2 W_1(t,r)}{\partial t\partial r}\\ for\quad t\in R_+,\quad r\in[0;a],\quad w\in\Omega\end{aligned}\right\}$$

(2.4)

Where, $f_1=\frac{\varphi_1-l_1-d-\alpha\varphi u}{\lambda_1}$, $g_1=\frac{c_1G_1}{\lambda_1}$, and

$a_1\to\sqrt{\frac{\lambda_1}{D_1}}\cdot a_1$.

We will use the notation P for the σ-algebra of F_t-progressively measurable subsets of R_+ x Ω and under some mathematical assumptions, we will consider the problems (2.3) and (2.4).

MATHEMATICAL ASSUMPTIONS

M_1: Both $f(t,r,w,z)$: R_+ x [0,a]x Ω x $R\to R$ and
$g(t,r,w,z)$: R_+ x [0,a] x Ω x $R\to R$
are $P\otimes B([0,a]\times R)$ measurable functions.

M_2: $\forall T,b>0,\exists C(T,b)$ such that

$$\sup_{0\le t\le T}\ \sup_{0\le r\le a}\ \sup_{0\le|z|\le b}\left(|f(t,r,w,z)|+|g(t,r,w.z)|\right)\le C(T,b)$$

a.s.

M_3: Both $f(t,r,w,z)$ and $g(t,r,w,z)$ satisfy a linear growth condition i.e. $\forall T>0,\ \exists K(T)$ such that $|f(t,r,w,z)|+|g(t,r,w,z)|\le K(T)(1+|z|)$, $\forall t\in[0,T]$, $r\in[0,a]$, $z\in R$ and almost all $w\in\Omega$.

M_4: Both $f(t,r,w,z)$ and $g(t,r,w,z)$ are continuous in $z\in R$.

M_5: $u_0=u_0(r, w)$ is a given non-negative F_0- measurable $C_0[0,a]$- valued random variable ($0\le u_0\le b$).

We state that $f(t,r,w,z)$ is *locally Lipschitz* if $\forall T,b>0,\exists K(T,b)$ is constant such that $|f(t,r,w,z_1)|+|g(t,r,w,z_2)|\le K(T)(z_2-z_1)$, $\forall t\in[0,T]$, $r\in[0,a]$, $z_1,z_2\in R$, with $z_1\vee z_2\le b$ and almost all $w\in\Omega$; $f(t,r,w,z)$ is *globally Lipschitz if* $K(T,b)$ does not depend on b.

The rigorous meaning of equations (2.3) and (2.4) are discussed next. Indeed, we do not expect solutions $u(t,r,w)$ and $v(t,r,w)$ to be differentiable in t or r. We regard (2.3) and (2.4) as a shorthand for some integral equations. Several authors, including Walsh [20], Da Prato and Zabczyk [5], have shown that, under some suitable assumptions, equation (2.3) has a unique *strong solution* in the following sense the random field $u=u(t,r,w)$ is a *strong solution* of equation (2.3) on the stochastic interval $t\in[0,\tau]$, where $\tau=\tau(w)$ is a stopping time, if

I. $u\Big|_{\{t<\tau\}}$ is $P\otimes B\big([0,a]\big)$ measurable, i.e. $u(t,r,w)$ is adapted process with filtration F_t,

II. $u(t,r,w)$ is continuous in $(t,r)\epsilon[0,\tau]$x[0,a] a.s., and

III. almost surely

$$\left.\begin{aligned}\int_0^a u(t,r,w)dr=\int_0^a u_0(r,w)\varphi(r)dr+\int_0^t\int_0^a u(s,r,w)\varphi^n(r)drds+\\ \int_0^t\int_0^a f(s,r,u)\varphi(r)drds+\int_0^t\int_0^a g(s,r,u)\varphi(r)W(ds,dr)\end{aligned}\right\}$$

(2.5)

It true for every, $\varphi(r)\in C_0^2\big[0,a\big]$ and for all $t\in[0,\tau)$; or equivalently, $u(\,t,r,w)$ satisfies the integral equation,

$$u(t,r,w)=\int_0^a u_0(r,w)G(t,r,\rho)d\rho+\int_0^t\int_0^a G(t-s,r,\rho)f(s,\rho,u)d\rho ds+\int_0^t\int_0^a G(t-s,r,\rho)g(s,\rho,u)W(ds,d\rho)$$

Where, $G(t,r,\rho)=\dfrac{1}{\sqrt{4\pi t}}\exp\left(\dfrac{-(\rho-r)^2}{4t}\right)$, is the Green's function associated to the operator $\dfrac{\partial^2}{\partial r^2}$ with Dirichlet boundary conditions.

The stochastic integral in (2.5) is a particular case of an integral with respect to a martingale measure as in the theory of Walsh [20]. If $P([\tau(w)=\infty])=1$ then u=u(t,*r,w,*) is a *global strong solution*. In this context, the following result from Donati-Martin and Pardoux [7] is needed.

Theorem 2.1. *Under the assumption, M_1-M_5, if f and g are globally Lipschitz, the equation* (2.3) *admits unique strong solution.*

3. THE EXISTENCE OF WEAK SOLUTIONS

We prove the existence of weak solutions to (2.3) via an approximation procedure and by a tightness argument.

Theorem 3.1. *Under the assumption M_1-M_5, the problem* (2.3) *admits a weak solution.*

The proof follows after a representation theorem for continuous orthogonal martingale measures. Let $\big\{I(t,r,w):t\in R_+,r\in\big[0,a\big],w\in\Omega\ \big\}$ be a $P\otimes B(R_+\times\big[0,a\big])$ measurable random field on R_+ x $[0,a]$ carried by a filtered probability space (Ω,F,F_t,P). Let L be a linear subspace of the Borel measurable functions Φ:$[0;a]\to R$ such that

1. L is closed with respect to the multiplication,
2. the σ-algebra of the subsets of R_+ x $[0,a]$ generated by L is $B(R_+$x $[0,a])$, and
3. $\int_0^T\int_0^a \Phi^2(r)I^2(t,r,w)drdt<\infty$ a.s.

The family of random variables $M=\big\{M(t,r,\Phi):t\in\big[0,T\big],w\in\Omega,\Phi\in L\ \big\}$ is called a continuous orthogonal martingale measure on $[0,T]$x$[0,a]$ with intensity $I^2(t,\ r,\ w)$ if $\forall\Phi\in L$ the random process $(M(t\ ,r,\ \Phi))_{0\le t\le T}$ is a continuous F_t-local martingale, such that almost surely

$$<M(\Phi),M(\Psi)>_t=\int_0^t\int_0^a \Phi(r)\Psi(r)I^2(s,r,w)drds\ ,\ \forall t\in\big[0,T\big],$$

for every $\Phi,\Psi\in L$, (see [15,17]).

The filtered probability space $\theta=(\Omega,\ F,\ F_t,\ P)$ is *reached* if it can carry a set-indexed space time white noise $W(t,\ r)$ on $[0,T]$ x $[0,a]$ which is independent of M.

We need the following representation theorem (see [8]).

Theorem 3.2. *If M is a continuous orthogonal martingale measure on* $[0,T]$x$[0,a]$ *with intensity $I^2(t,r,w)$ carried by a reach filtered probability space θ, then there exist a set-indexed space-time white noise $W(t,r)$ on R_+x$[0,a]$, such that,*

$$M(t,w,\Phi)=\int_0^t\int_0^a \Phi(r)\Psi(r)I(s,r,w)W(ds,dr)\ ,\ \forall t\in\big[0,T\big].$$

Proof of theorem 3.1. Let $f_n=f_n(t,r,w,z)$ and $g_n=g_n(t,r,w,z)$ be two sequences of Lipschitz functions converging uniformly to $f=f(t,r,w,z)$ and $g=g(t,r,w,z)$ respectively for $z\in R$. Also assume that both f_n and g_n satisfy M_3 with a constant K (T) independent on n. For example, $f_n=\int_R f(t,r,w,z-x/n)\rho(x)d(x)$ and $g_n=g(t,r,w,z-x/n)(x)d(x)$, where

ρ: $R\to R_+$ is a smooth kernel supported on $[0,a]$, such that $\int_R\rho(x)d(x)=1$. Then according Theorem 2.1 there exist a unique strong solution of the equation (2.3) with f_n and g_n, for each $n\ge1$. Using the same argument as in Walsh [20] or Da Prato and Zabczyk [5], one can check the moment condition:

for each $T>0$, $E\,|u_n(t,r)-u_n(s,\rho)|^\sigma\le C(|t-r|^2+|r-\rho|^2)^{2+\epsilon}$ for some constants $C>0$, $\varepsilon>0$, $\sigma\ge1$ and all $t,\ r\in[0,T]$; $r,\ \rho\in[0,a]$, with C not depending on n. Now we can apply Kolmogorov's test to the sequence of random fields $\{u_n(t,\ r),W(\ t,\ r):\ t\in[0.T],r\in[0,a]\}$, and we find

a sequence of random fields $(\hat{u}_{n'}, \hat{W}_{n'})$ on a filtered probability space for a sequence $n' \to \infty$ such that the finite dimensional distributions of $(\hat{u}_{n'}, \hat{W}_{n'})$ coincide with the finite dimensional distributions of $(u_{n'}, W)$ for each n', and $(\hat{u}_{n'}, \hat{W}_{n'})$ converges almost surely to a random field $(\hat{u}, \hat{W})$ in $C([0,T]\text{x}[0,a];R^2)$.

We choose $L = C_0^2[0,a]$ and find that

$$\left.\begin{aligned}(\hat{u}_n(t),\Phi) = (\hat{u}_{0,n},\Phi) + \int_0^t [(\hat{u}_n(s)\Phi^n(r)) + (f_n(\hat{u}_n(s)),\Phi)]ds + \\ + \int_0^t\int_0^a g_n(s,r,\hat{u}_n(s,r))\Phi(r)\hat{W}_n(ds,dr) \quad a.s.\end{aligned}\right\} \tag{3.1}$$

for all $\forall t \in [0,T]$, $\forall \Phi \in L$, and for every $n=n'$ (we can write n instead of n' only for notational convenience). Choosing a sequence which converges in distribution (i.e. $n \to \infty$) we obtain a solution $\hat{u}$ to the equation

$$(\hat{u}(t),\Phi) = (\hat{u}_0,\Phi) + \int_0^t [(\hat{u}(s),\Phi^n(r)) + (f(\hat{u}(s),\Phi(r))]ds + M(t,\Phi), \tag{3.2}$$

Where, $M(t,\Phi): t \in [0,T], \Phi \in L = C_0^2[0,a]$ is the almost surely limit in $C([0,T])$ of the random processes

$$M_n(t,\Phi) = \int_0^t\int_0^a g_n(s,r,\hat{u}_n(s,r))\Phi(r)\hat{W}_n(ds,dr).$$

It is clear that the limit $lim_{n\to\infty} M_n(t,\Phi) = M(t,\Phi)$ exist (because all the other terms in (3.1) have the corresponding limits in (3.2)) and $\forall n \in N$, $\forall \Phi \in L$, the random process $(M_n(t,\Phi))_{t\in[0,T]}$ is a continuous martingale with quadratic variation

$$< M_n(t,\Phi) >_t = \int_0^t\int_0^a |g_n(s,r,\hat{u}_n(s,r))|^2 |\Phi(r)|^2 dsdr.$$

Hence, $(M(t,\Phi))_{t\in[0,T]}$ is a continuous martingale with quadratic variation

$$< M(t,\Phi) >_t = \int_0^t\int_0^a |g(s,r,\hat{u}(s,r))|^2 |\Phi(r)|^2 dsdr. \tag{3.3}$$

and $M = \{M(t,\Phi): t \in [0,T], \Phi \in L\}$ is a continuous orthogonal martingale measure with intensity, $l^2(s,r) = |g(s,r,\hat{u}(s,r))|^2$

Thus, we prove the existence of the solution of the martingale problem (3.2)-(3.3) corresponding to (2.3) and consequently apply Theorem 3.2 representing M as,

$$M(t,\Phi) = \int_0^t\int_0^a g(s,r,\hat{u}(s,r))W(ds,dr),$$

Where $W(t,r)$ is a set-indexed white noise on $[0,T]\text{x}[0,a]$. We assume that the filtered probability space θ is reach. Otherwise, we can take an extension of θ.

We also use the assumption

M_6:The random field $f_2 = f_2(t,r,w)$: $t \epsilon R_+$, $r \epsilon [0,a]$, $\omega \epsilon \Omega$, is $P \otimes B[0,a]$, measurable and there exists a deterministic function $F(t) \in L^1_{loc}(R_+)$ such that

$$\int_0^a f_2^2(t,r,w)dr \le F(t), \quad \forall t \ge 0, \quad \text{a.s.}$$

Remark 1.Theorem 3.1 still holds even if $f(t,r,w,z)$ is replaced by $f(t,r,w,z) + f_2(t,r,w,)$ Where f_2 satisfies M_6. The proof is similar to the proof of Theorem 3.1.

Uniqueness for weak solutions to (2.3) is important for justifying that the mathematical model is viable and is a useful step in showing the numerical approximating solutions converges. Using the moment duality method developed by S. Athreya and R. Tribe [1] we can prove the *uniqueness in law* (*weak uniqueness*) for some special cases.

Theorem 3.3. *Assume that* (θ, W, u) *is a bounded weak solution to (2.3)*

$$0 \le u \le b \quad \text{for all } t > 0,\ r \in [0,a],\ P\text{ - a.s,}$$

$f(u)$ *and* $g^2(u)$ *are analytic functions with respective power series representation*

$$f(u) = \sum_0^\infty f_k u_k, \quad \sigma(u) = g^2(u) = \sum_0^\infty \sigma_k u_k$$

Assume that the power series of f and g^2 *are convergent in the interval* $[-R,R]$ *for some* $R>b$ *Assume that there is* $x>b$ *such that*

$$f_1 < -\sum_{k\ne 1} |f_k| x^{k-1} \quad \text{and} \quad \sigma_2 < -\sum_{k\ne 2} |\sigma_k| x^{k-2}.$$

Under these assumptions, there is a unique probability measure μ *on the space* C^+_{tem} *so that* $u=u(t,r,w)$ *has law* μ *whenever* (θ, W, u) *is a weak solution to (2.3) on some filtered probability space* (Ω, F, F_t, P). *If* $f=0$ *then*

the parts of the hypotheses that refer to f may be removed.

The proof is omitted since it is standard (see [1]). Girsanov's theorem can sometimes be used to alter the drift term

$f(u) = f^{+}(u) - f^{-}(u)$ to $\hat{f}(u) = f^{+}(u) - f^{-}(b)u.$

However, many drift terms cannot be treated by this method. The linear scaling defined by the formula $v=v(t,r,w)=Bu(C_1t,C_2r,w)$, where, $B \neq 0$, $C_1 > 0$ and $C_2 > 0$ does not change our ability to establish uniqueness in law for the weak solutions to (2.3), using Theorem 3.3.

CONCLUSION

We believe in the effectiveness of stochastic partial differential equations and martingale approach in modeling of the tumor growth after curative resection of a tumor, as well as at the early stages of tumor growth. The multiplicative space-time white noise term for random independent interactions between tumor cells, immune system cells and anticancer drugs is introduced in this paper. We prove the weak existence and uniqueness in law for the continuous random field $u(t,r,w)$ which represents the density number of drug sensitive tumor cells. The obtained theoretical results and computer simulations should lead to the better understanding of the key parameters in which the final disease is depended.

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