$$Y(r,0,t) = \int_0^t \lim_{s\to\infty} \int_{-s}^{s} U[(V_x)_{T,\varepsilon,4,\xi},\omega]\, \frac{\partial \Psi_2(r,0,\omega)}{\partial r}\, e^{\left(i\omega + \frac{E}{3\eta}\right)\tau}\, d\omega d\tau.$$

Since $U[(V_x)_{T,\varepsilon,4,\xi},\omega]$ is $O(|\omega|^{-4})$ for ω real, $\omega \to \infty$ and since $\partial\Psi_2(r,0,\omega)/\partial r$ is $O(|\omega|)$, the order of integration may be reversed. Since, for $T > |t| + \gamma + \varepsilon$, the integral is independent of T, a $\lim\limits_{T\to\infty}$-sign may again be prefixed.

Lemma 7.9: $\displaystyle\int_0^t e^{\frac{E}{3\eta}\tau} \frac{\partial}{\partial r} \left\{\lim_{T\to\infty} \lim_{s\to\infty} \int_{-s}^{s} U[(V_x)_{T,\varepsilon,4,\xi},\omega]\, e^{i\omega\tau} F_2(r,0,\omega)\right\} d\omega d\tau$

and

$$\lim_{T\to\infty}\lim_{s\to\infty} \int_{-s}^{s} \frac{\partial}{\partial r} [F_2(r,0,\omega)\, U[(V_x)_{T,\varepsilon,4,\xi},\omega]\, \frac{e^{\left(i\omega + \frac{E}{3\eta}\right)t} - 1}{i\omega + \frac{E}{3\eta}}\, d\omega ,$$

exist and are equal.

Proof: Apply the representation (6. 18) to the partial derivative in the first integral, substituting F_2 for the function f from Theorem 2, r for x, V_x for v, $m' = 0$, $n' = 1$. By [2] from the proof of Theorem 2, Lemma 3.1 may now be applied,. The application concludes the proof of the lemma.

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ASUPRA UNEI GENERALIZĂRI A INTEGRALEI DE TIP FOURIER
ŞI APLICAŢIILE ACESTEIA LA UNELE PROBLEME PE CONTUR

Rezumat

De multe ori soluţiile unor ecuaţii cu derivate parţiale sînt date sub forma (1.1). Pentru a evita unele dificultăţi ce se ivesc datorită condiţiei ca (1.3) să conveargă, se studiază următoarele probleme: a) Cînd există limita (1.7) cu $Y(X,t,T)$ dat de (1.6) şi U_T dat de (1.5); b) Cînd este această funcţie derivabilă; c) Cînd se pot obţine aceste derivate derivînd funcţia Y.

După ce se dau condiţii în care răspunsurile la aceste întrebări sînt afirmative, se studiază în § 7 problema curgerii unui fluid Maxwell, în jurul unei sfere rigide, cu ajutorul ecuaţiei (7.1).

STOCHASTIC INTEGRAL EQUATIONS IN ENGINEERING AND BIOLOGICAL SCIENCES

BY

CHRIS P. TSOKOS*

1.0. Introduction. In mathematical models of phenomena occurring in the general areas of engineering, biological and physical sciences, random or stochastic equations appear frequently, [4], [10] [11]. The aim of this talk is to formulate stochastic models in fluid mechanics and chemotherapy which lead to stochastic integral equations of the form

$$v(t;\omega) = \int_0^t \varphi(v(\tau;\omega), t, ;\tau;\omega)d\tau, \qquad (1.1)$$

and

$$x(t;\omega) = h(t;\omega) + \int_0^t k(s,\ x(s;\omega);\ \omega)ds. \qquad (1.2)$$

We shall also be concerned with the existence of a random solution and its physical interpretation in the aforementioned models.

2.0. On a Stochastic Model for Fluid Mechanics. Consider a tagged material point in a continuous fluid in turbulent motion. The location of the designated point at time $t>0$, is a vector-valued stochastic variable, $\mathbf{v}(t;\omega)$, $\omega \in \Omega$ [where Ω is the supporting set of the underlying probability

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space (Ω, A, μ)]. At location $\mathbf{v}(t;\omega)$, the velocity of the point is given by the Eulerian velocity field $\eta(\mathbf{v}(t;\omega), t;\omega)$, a vector valued random variable for each $\mathbf{v}$ and $t \geq 0$. The Eulerian approach to describing flow in fluid mechanics is that the velocity of a point in a continuous fluid moving by a fixed position at any given time $t \geq 0$ can be given. However, when the flow is turbulent, the velocity is random and we are phased with the problem of determining $\mathbf{v}(t;\omega)$ if the statistical properties of $\eta(\mathbf{v}(t;\omega)t;\omega)$ are known. The location of the designated point is given by the stochastic integral equation of the form

$$\mathbf{v}(t;\omega) = \int_0^t \eta(\mathbf{v}(\tau;\omega), \tau;\omega)\, d\tau, \tag{2.1}$$

where :

(*i*) $\omega \in \Omega$;

(*ii*) $\mathbf{v}(t;\omega)$ is the unknown vector-valued random function which gives the coordinates of the position of the tagged point in the fluid for each time $t \geq 0$;

(*iii*) $\eta(\mathbf{v}(t;\omega), t;\omega)$ is the Eulerian velocity field specified in laboratory coordinator for each $t \geq 0$.

Lumley, [12], studied a discretized version of the stochastic integral equation (2. 1). In this paper we shall give conditions under which equation (2. 1) admits a random solution for each $t \geq 0$. By a *random solution* of equation (2. 1) we shall mean the following: The random vector-valued function $\mathbf{v}(t;\omega)$ is a *random solution* of the stochastic integral equation (2. 1) if for each fixed $t \geq 0$, $\mathbf{v}(t;\omega)$ is a vector random variable and satisfies (2. 1) almost everywhere.

We shall study the problem by considering a stochastic integral equation of the form

$$\mathbf{v}(t;\omega) = \int_0^t \psi(\mathbf{v}(\tau;\omega), t, \tau;\omega)\, d\tau, \tag{2.2}$$

where $\mathbf{v}(t;\omega)$ is the unknown vector-valued random variable for each $t \geq 0$, and $\psi(\mathbf{v}(\tau;\omega), t, \tau, \omega)$ is the stochastic kernel which equals to $\eta(\mathbf{v}(t;\omega), \tau, \omega)$ for $0 \leq \tau \leq t < \infty$ and 0, elsewhere. We shall assume that $\mathbf{v}(t;\omega)$ is a three-component vector-valued continuous function from $R_+ = [0, \infty)$ into the space $L_p(\Omega, A, \mu)$, $1 \leq p < \infty$, that is, for each $t \in R_+$,

$$\|\mathbf{v}(t;\omega)\|_p = \left\{ \int_\Omega |\mathbf{v}(t;\omega)|^p\, d\mu(\omega) \right\}^{\frac{1}{p}} < \infty.$$

Thus for each $t \in R_+$, $\omega \in \Omega$, $\mathbf{v}(t;\omega)$ is a point in threedimensional Euclid-dean space, $(v_1(t;\omega), v_2(t;\omega), v_3(t;\omega))$, and

$$|\mathbf{v}(t;\omega)|^2 = v_1^2(t;\omega) + v_2^2(t;\omega) + v_3^2(t;\omega).$$

We will assume that ψ is a function such that for each fixed pair (t, τ) in the set

$$\xi = \{(t, \tau) : 0 \leq \tau \leq t < \infty\},$$

$\psi(\mathbf{v}(\tau;\omega), t, \tau, \omega)$, $\omega \in \Omega$, is continuous in $\mathbf{v}$, for each $\mathbf{v}$, $\omega \in \Omega$, $\psi(\mathbf{v}, t, \tau;\omega)$ is a continuous function on ξ. Thus ψ is of the form

$$(\psi_1(\mathbf{v}, t, \tau;\omega),\ \psi_2(\mathbf{v}, t, \tau;\omega),\ \psi_3(\mathbf{v}, t, \tau;\omega))$$

a point in three-dimensional Euclidean space for each fixed $\mathbf{v}$, (t, τ), and $\omega \in \Omega$, and for each fixed $\mathbf{v}$, $(t, \tau) \in \xi$, we have $\psi(\mathbf{v}, t, \tau;\omega) \in L_p(\Omega, A, \mu)$ with $|\psi(\mathbf{v}(\tau;\omega), t, \tau;\omega)|$ defined as for $\mathbf{v}(t;\omega)$ above.

We shall denote $C_p(R_+, L_p(\Omega, A, \mu)) = C_p$ the space of all three-component vector-valued functions from R_+ into $L_p(\Omega, A, \mu)$ with the topology of uniform convergence on each compact interval $[0, T]$, $T > 0$. That is, the sequence $\mathbf{v}_n(t;\omega) \in C_p$ converges to $\mathbf{v}(t;\omega) \in C_p$ iff

$$\lim_{n \to \infty} \left\{ \int_\Omega |\mathbf{v}_n(t;\omega) - \mathbf{v}(t;\omega)|^p d\,\mu(\omega) \right\}^{\frac{1}{p}} = 0,$$

uniformly on every compact interval $[0, T]$.

Let B and D be a pair of Banach spaces such that $B, D \subset C_p$ and assume that T is a linear operator from C_p into C_p. The pair of Banach spaces (D, B) is said to be *admissible* with respect to T if $TD \subset B$.

The following lemma will be useful in the aim of the paper.

Lemma 1.1. *Assume T is a continuous operator from C_p into itself. If the pair of Banach spaces B and D are stronger than C_p and if (D, B) is admissible with respect to T, then T is a continuous operator from D into B.*

Since T is a continuous operator, it is bounded, [2], and one can find a constant $K > 0$ such that

$$\|(T\mathbf{x})(t;\omega)\|_B \leq K \|\mathbf{x}(t;\omega)\|_D.$$

Theorem 2.1. *Suppose that the stochastic integral equation (2.2) satisfies the following conditions:*

(*i*) *B and D are Banach spaces stronger than C_p, and the pair (D, B) is admissible with respect to the operator T given by*

$$(T\mathbf{v})(t;\omega) = \int_0^t \mathbf{v}(\tau;\omega)\, d\tau;$$

(*ii*)

$$\psi(\mathrm{v}, t, \tau, \omega) = \begin{cases} \eta(\mathrm{v}, \tau; \omega), & 0 \leq \tau \leq t < \infty \\ 0 & , \text{elsewhere} \end{cases}$$

is a mapping from the set

$$E = \{\mathrm{v}(t;\omega)\colon\ \mathrm{v}(t;\omega) \in B, \|\mathrm{v}(t;\omega)\|_B \leq \rho\}$$

into the space D, for $\rho \geq 0$;

(*iii*) $\|\eta(\mathrm{v}(t;\omega), t; \omega\|_D \leq \rho/K$, *where* K *is the norm of* T.

Then there exists at least one random solution of the stochastic integral equation (2.2).

Proof: Let U be an operator from E into B of the form

$$(U\mathrm{v})(t;\omega) = \int_0^t \eta(\mathrm{v}(\tau;\omega), \tau; \omega)\, d\tau.$$

Thus U is a continuous mapping from E to B, since the function η is continuous in v. The set E is convex, closed and bounded. If for $0 < a < 1$, then for $\mathrm{v}_1(t;\omega)$, $\mathrm{v}_2(t;\omega) \in E$, we have

$$\|\mathrm{v}(t;\omega)\|_B = \|a\mathrm{v}_1(t;\omega) + (1-a)\mathrm{v}_2(t;\omega)\|_B \leq a\rho + (1-a)\rho = \rho.$$

thus a convex combination of two elements of E is also an element of E Suppose that $\{\mathrm{v}_n(t;\omega)\}$ is a sequence in E converging to a point $\mathrm{v}(t;\omega) \in B$, then we have

$$\|\mathrm{v}(t;\omega)\|_B \leq \|\mathrm{v}(t;\omega) - \mathrm{v}_n(t;\omega)\|_B + \|\mathrm{v}_n(t;\omega)\|_B \leq \|\mathrm{v}(t;\omega) - \mathrm{v}_n(t;\omega)\|_B + \rho \to \rho$$

as $n \to \infty$.

Therefore, $\mathrm{v}(t;\omega) \in E$ and E is closed. By definition, E is bounded and since it is a subset of a Banach space, it is compact.

We proceed to show that $U(E) \subset E$. From condition (*iii*) it is clear that

$$\|(U\mathrm{v})(t;\omega)\|_B = \|\int_0^t \eta(\mathrm{v}(\tau;\omega), \tau; \omega)d\tau\|_B \leq K\|\eta(\mathrm{v}(t;\omega), t; \omega)\|_D \leq \rho.$$

The operator U is continuous and from the fact that a continuous image of a compact set is compact, then we have $U(E)$ is compact. In view of Schauder's Fixed Point Theorem, [1], there exist at least one point $\mathrm{v}(t;\omega) \in E$ such that

$$(U\mathrm{v})(t;\omega) = \int_0^t \eta(\mathrm{v}(\tau;\omega), \tau; \omega)\, d\tau = \mathrm{v}(t;\omega)$$

for each $t \in R_+$. This theorem applies to any k component vector valued functions as well. The components of η record the random rate of change of the coordinator of the tagged point at time t, $\delta v_i(t;\omega)/\delta t$, $i = 1, 2, 3$, and the length of η, that is, $|\eta(\mathrm{v}, t; \omega)|$, records the random speed of the tagged material point at time $t \geq 0$.

3.0. On a Stochastic Model for Chemotherapy. We shall begin by studying the existence of a random solution of a stochastic integral equation which will be of importance in the solution of the chemotherapy model. This equation is of the form

$$x(t;\omega) = h(t;\omega) + \int_0^t k(s, x(s;\omega); \omega)\,ds, \tag{3.1}$$

where;

(*i*) $\omega \in \Omega$;

(*ii*) $x(t;\omega)$ is the unknown random variable with $t \in [0, M]$ for $0 < M < \infty$;

(*iii*) $h(t;\omega)$ is the stochastic free term;

(*iv*) $k(t, x(t;\omega); \omega)$ is the stochastic kernel defined on $[0, M] \times (-\infty, \infty) \times \Omega$.

We shall assume that $x(t;\omega)$, $h(t;\omega)$, and $k(t, x(t;\omega); \omega)$ are real-valued functions. Also for each $t \in [0, M]$ it will be required that $x(t;\omega)$ and $h(t;\omega)$ ar in space $L_p(\Omega, A, \mu)$, $1 \leq p < \infty$, and for each $x \in (-\infty, \infty)$ the kernel $k(t, x; \omega)$ is product measurable on $[0, M] \times \Omega$, and for each $t \in [0, M]$ and $x \in (-\infty, \infty)$, $k(t, x; \omega) \in L_p(\Omega, A, \mu)$. It is also assumed that $x(t;\omega)$ and $h(t;\omega)$ are product measurable on $[0, M] \times \Omega$ (with respect to Lebesgue measure on $[0, M]$).

Let $1/p + 1/q = 1$ or $q = -p/(1-p)$, $p > 1$. The sequence $\{x_n(\omega)\}$, $\omega \in \Omega$, *converges weakly* to $x(\omega)$ in $L_p(\Omega, A, \mu)$, $p > 1$, if

$$\lim_{n\to\infty} \int_\Omega x_n(\omega)\, h(\omega)\, d\mu(\omega) = \int_\Omega x(\omega)\, h(\omega)\, d\mu(\omega), \tag{3.2}$$

for every $h \in L_q(\Omega, A, \mu)$. If $p = 1$, then $\{x_n(\omega)\}$ *converges weakly* to $x(\omega)$ in $L_1(\Omega, A, \mu)$ if (3.2) holds for every bounded measurable function h on Ω.

Theorem 3.1. *We consider the random integral equation* (3.1) *under the following conditions:*

(*i*) *The kernel* $k(t, x(t;\omega); \omega)$ *is a continuous function of* t *and* x, $t \in [0, \infty)$, $x \in (-\infty, \infty)$, *for each* $\omega \in \Omega$, *and* $k(t, x; \omega) \in L_p(\Omega, A, \mu)$, $1 \leq p < \infty$, *for each* t *and* x;

(*ii*) *For all* $t \in [0, M]$

$$\sup_x |(k, t, x; \omega)| \leq g(\omega) \in L_p(\Omega, A, \mu).$$

$1 \leq p < \infty$;

(iii) $h(t;\omega)$ is a continuous function from $[0, M]$ into $L_p(\Omega, A, \mu)$, and for each $t \in [0, M]$, $0 < M < \infty$, there exists a constant $N_M > 0$ such that

$$|h(t;\omega)| + \int_0^t \sup_x |k(s, x; \omega)|\, ds \leqslant N_M < \infty$$

for each $\omega \in \Omega$;

(iv) The kernel satisfies the following weak continuity property: If $x_n(\omega)$ converges weakly to $x(\omega)$ in $L_p(\Omega, A, \mu)$, $1 \leqslant p < \infty$, then $k(t, x_n(\omega); \omega)$ converges weakly to $k(t, x(\omega); \omega)$ in $L_p(\Omega, A, \mu)$ for each $t \in [0, M]$.

Then, for $t \in [0, M]$, $0 < M < \infty$, there exists a random solution of the random integral equation (3.1).

Proof: For $t \in [0, M]$, we define the sequence

$$x_0(t;\omega) = h(t;\omega)$$

and

$$x_n = \begin{cases} x_0(t;\omega), \text{ if } 0 \leqslant t \leqslant \frac{1}{n} \\ x_0(t;\omega) + \int_0^{t-\frac{1}{n}} k(s, x_{n-1}(s;\omega);\omega)\, ds \text{ if } \frac{m}{n} \leqslant t \leqslant \frac{m+1}{n}\ 1 \leqslant m \leqslant mn - 1 \end{cases}$$

for $n \geqslant 1$.

Since $h(t;\omega) \in L_p(\Omega, A, \mu)$, $1 \leqslant p < \infty$, for each $t \in [0, M]$, then $x_0(t;\omega) \in L_p(\Omega, A, \mu)$. Thus $x_n(t;\omega)$, $n \geqslant 1$, is in $L_p(\Omega, A, \mu)$, since by condition (*ii*) and an extension of Minkowski's inequality [3] for $t \in [0, M]$, we have

$$\left\{\int_\Omega \left|\int_0^t k(s, x_n(s;\omega);\omega)\, ds\right|^p d\mu(\omega)\right\}^{\frac{1}{p}} \leqslant \int_0^t \left[\int_\Omega |k(s, x_n(s;\omega);\omega)|^p d\mu(\omega)\right]^{\frac{1}{p}} ds \leqslant$$

$$\leqslant \int_0^t \left[\int_\Omega |g(\omega)|^p d\mu(\omega)\right]^{\frac{1}{p}} ds < \infty.$$

Then

$$\left\{\int_\Omega |x_n(t;\omega)|^p d\mu(\omega)\right\}^{\frac{1}{p}} = \left\{\int_\Omega \left|h(t;\omega) + \int_0^t k(s, x(s;\omega);\omega)\, ds\right|^p d\mu(\omega)\right\}^{\frac{1}{p}} \leqslant$$

$$\leqslant \left\{\int_\Omega |h(t;\omega)|^p d\mu(\omega)\right\}^{\frac{1}{p}} + \left\{\int_\Omega \left|k(s, x(s;\omega);\omega)\, ds\right|^p d\mu(\omega)\right\}^{\frac{1}{p}} < +\infty$$

by Minkowski's inequality, the above result and the fact that $h(t;\omega) \in L_p(\Omega, A, \mu)$ for each $t \in [0, M]$.

Since $h(t;\omega)$ is continuous from $[0, M]$ into $L_p(\Omega, A, \mu)$, $1 \leqslant p < \infty$, we have that the family $\{x_n(t;\omega)\}_{n=0}^{\infty}$ is an equicontinuous family of functions from $[0, M]$ into $L_p(\Omega, A, \mu)$. That is, let $\varepsilon > 0$ be given and $n \geqslant 0$ fixed, but arbitrary. Then for $t_1, t_2 \in [0, M]$,

$$|x_n(t_1;\omega) - x_n(t_2;\omega)| = \left|\int_0^{t_1-\frac{1}{n}} k(s, x_{n-1}(s;\omega);\omega)\, ds - \int_0^{t_2-\frac{1}{n}} k(s, x_{n-1}(s;\omega);\omega)\, ds + \right.$$

$$\left. + x_0(t_1;\omega) - x_0(t_2;\omega)\right| \leqslant \left|\int_0^{t_1-\frac{1}{n}} k(s, x_{n-1}(s;\omega);\omega)\, ds - \int_0^{t_2-\frac{1}{n}} k(s, x_{n-1}(s;\omega);\omega)\, ds\right|$$

$$+ |h(t_1;\omega) - h(t_2;\omega)|.$$

for $\omega \in \Omega$. Therefore we can find a $\delta > 0$ such that for $|t_1 - t_2| < \delta$, we have

$$|h(t_1;\omega) - h(t_2;\omega)| < \frac{\varepsilon}{2}$$

and

$$\left|\int_0^{t_1-\frac{1}{n}} k(s, x_{n-1}(s;\omega);\omega)\, ds - \int_0^{t_2-\frac{1}{n}} k(s, x_{n-1}(s;\omega);\omega)\, ds\right| < \frac{\varepsilon}{2}.$$

Hence, for every $\varepsilon > 0$, we can find a $\delta > 0$ such that whenever $|t_1 - t_2| < \delta$, we have for $\omega \in \Omega$

$$|x_n(t_1;\omega) - x_n(t_2;\omega)| < \varepsilon.$$

Since $n \geqslant 0$ is arbitrary, the $x_n(t;\omega)$ as functions from $[0, M]$ into $L_p(\Omega, A, \mu)$ are equicontinuous.

Furthermore, since $h(t;\omega)$ is product measurable on $[0, M] \times \Omega$ and $k(t, x;\omega)$ is product measurable on $[0, M] \times \Omega$ for each x, then $x_n(t;\omega)$ is product measurable on $[0, M] \times \Omega$ for all $n \geqslant 0$.

For $t \in [0, M]$, we have by condition (*iii*) that

$$|x(t;\omega)| \leqslant |h(t;\omega)| + \int_0^s |k(s, x(s;\omega);\omega)|\, ds \leqslant |h(t;\omega)| + \int_0^t \sup |k(s, x;\omega)|\, ds \leqslant$$

$$\leqslant N_M < \infty,$$

for any $x(t;\omega)$. The sequence $\{x_n(t;\omega)\}$ satisfies the conditions of the Arzelà-Ascoli Theorem, [9], and hence there exists a subsequence $\{x_{n_i}(t;\omega)\}$ that converges weakly in $L_p(\Omega, A, \mu)$ to a product measurable function $x(t;\omega)$ from $[0, M]$ into $L_p(\Omega, A, \mu)$ for each $t \in [0, M]$. Thus, by condition (*iv*), for each $t \in [0, M]$, $x(t;\omega)$ satisfies the equation

$$x(t;\omega) = h(t;\omega) + \int_0^t k(s, x(s;\omega);\omega)ds,$$

μ-a.e. Hence, there exists a random solution of equation (3.1) for each $t \in [0, M]$.

Bellman, Jacquez and Kalaba [5], [6], [7], [8] developed a deterministic version of a one-organ model for chemotherapy. We shall develop here a stochastic version of their model and show that a *semi-random* solution exists, [15]. That is, the random function $x(t;\omega)$ will be called a *random solution* of (3.1) on the interval $[0,M]$ if for every $t \in [0, M]$, $x(t;\omega)$ satisfies equation (3.1) μ-a.e., and it is a random variable for each $t \in [0, M]$. The function $x(t;\omega)$ will be called a *semi-random solution* of (3.1) if there exists a τ, $0<\tau<M$, such that the following conditions hold:

(*i*) For each fixed t, $0 \leqslant t < \tau$, $x(t;\omega)$ is a deterministic function of t, that is, $x(t;\omega) = \zeta(t)$ μ-a.e. and satisfies equation (3.1);

(*ii*) For every fixed t, $\tau \leqslant t \leqslant M$, $x(t;\omega)$ is a random solution of (3.1).

We consider a closed system with a simplified heart, one organ or capillary bed, and assume that the recirculation of the blood is at constant rate of flow, where the heart is considered as a mixing chamber of constant volume. The flow of blood is considered as „slug" flow (no mixing in the vessels). It is assumed that an injection of drug is given to the system directly at the entrance of the heart producing a known concentration of drug in the plasma. That is, drug molecules are dissolved in the blood plasma. Also, as the blood passes through the capillary bed or organ, the particles of drug are assumed to enter the extracellular space only by the process of diffusion through the capillary walls, since Pappenheimer, et al., [8] showed filtering to be negligible.

Since it is impossible to know the point-by-point concentration of drug in the plasma and extracellular space at any given time after injection, for a given experiment measurements of drug concentration should be made at a set of points in a given area of the system at the same instant of time, and the *mean value* of this set of experimental values should be used as the concentration of drug in that area of the system. For example, several measurements may be taken at points between the heart exit and the entrance to the capillary bed at time $t>0$, since the concentration is considered fairly uniform in certain areas of the system, [5], [7]. It is realistic to assume that this mean value estimates the true state of nature at the given time $t>0$, and if another initial injection is given in the same system and the measurements are repeated under the same conditions as above, a different *mean value* would result. Thus, the concentration of the compound in plasma in given areas of the system is more realistically considered as a random function of time rather than a deterministic one.

For $t \geqslant 0$, we shall use the following notation: $u(s, t;\omega)$ is the concentration of drug in moles per unit volume at point s in the capillary at time $t \geqslant 0$, $\omega \in \Omega$; c is the constant volume flow rate of plasma in the capillary bed; and l is the mean length of capillary in the capillary bed. We assume a macroscopic point of view in that all capillaries in the capillary bed are lumped together into one capillary of length l, total volume flow rate c, and total surface area A_c equal to that of all the capillaries combined.

For a one-organ system maintained by a simplified heart, let the heart be considered a mixing chamber of constant volume given by

$$V^* = \frac{V_e}{\ln(1 + V_e/V_r)},$$

where V_r is the residual volume of the heart, and V_e is the ejection volume and constant entering and leaving flow rates c, [7]. This is obtained by representing the concentration of drug in the volume of plasma ejected by the heart at time t, $\gamma(t)$, as a function of V_e and V_r and of the concentration of drug at time zero, γ_0, in the residual blood in the heart, that is,

$$\gamma(t) = \gamma_0 \exp[-ct/V^*], t \geqslant 0.$$

Suppose that an initial injection is given at a constant rate directly at the entrance of the heart which gives concentration $u_I(t)$, $0 \leqslant t \leqslant t_I$, entering the heart, where t_I is the duration of the injection. Let the time required for blood to flow from the exit of the capillary bed or organ to the entrance of the heart be $\gamma > 0$, that is, a circulation time lag. Also, let γ be the time required for blood to flow from the exit of the heart to the entrance of the organ. Thus, plasma containing a concentration of drug reaches the organ after time γ, and while flowing through the organ or capillary bed diffusion through the capillary walls into the extracellular space takes place. Hence after time γ, the concentration of drug in plasma at the entrance of the heart is a random variable, $u_R(t;\omega)$, due to this diffusion process and recirculation of the blood, and is given by

$$u_R(t;\omega) = \begin{cases} 0 & , \ t<0 \\ u_I(t) & , \ 0 \leqslant t < \gamma \\ u_I(t) + u(l, t-\gamma;\omega), & t \geqslant \gamma, \end{cases} \tag{3.3}$$

where $u(l, t;\omega)$ is the concentration of drug in plasma leaving the capillary bed or organ at time t, a random variable for each $t \geqslant 0$, and $u_I(t) = 0$ for $t > t_I$. Let the concentration of drug in plasma leaving the heart be denoted by $u_L(t;\omega)$. Then $u_L(t;\omega)$ satisfies the integral equation,

$$u_L(t;\omega) = u_L(0;\omega) + \frac{C}{V^*}\int_0^t [u_R(s;\omega) - u_L(s;\omega)]\,ds,\ t \geq 0,$$

where $u_L(0;\omega) = 0$. Hence,

$$u_L(t;\omega) = \int_0^t \frac{C}{V^*}[u_R(s;\omega) - u_L(s;\omega)]\,ds,\ t \geq 0. \tag{3.4}$$

Then the concentration of drug entering the organ at time t is given by

$$u(0,\ t;\ \omega) = \begin{cases} 0, & 0 \leq t < \gamma \\ u_L(t-\gamma;\ \omega), & t \geq \gamma. \end{cases} \tag{3.5}$$

Since $u_R(t;\omega)$ is a deterministic function of time for $0 \leq t < \gamma$ when the initial concentration wave (a square wave) is known, then $u_L(t;\omega)$ is also deterministic for $t < \gamma$. However, after time γ when the diffusion process in the organ is begun, due to recirculation $u_R(t;\omega)$ is a random function of time, and hence so is $u_L(t;\omega)$. Thus, equation (3. 4) is a semi-stochastic integral equation of the form (3. 1).

Substituting (3. 3) into equation (3. 4), we have

$$\begin{aligned} u_L(t;\omega) &= \int_0^t \frac{c}{V^*}[u_I(s) + u(l,s-\gamma;\omega) - u_L(s;\omega)]\,ds \\ &= \int_0^{T(t)} \frac{c}{V^*}u_I(s)\,ds + \int_0^t -\frac{c}{V^*}[u_L(s;\omega) - u(l,s-\gamma;\omega)]\,ds \\ &= G(t) + \int_0^t k(s, u_L(s;\omega);\omega)\,ds, \end{aligned} \tag{3. 6}$$

where

$$G(t) = \int_0^{T(t)} \frac{c}{V^*}u_I(s)\,ds,\quad T(t) = \begin{cases} t, & \text{if } 0 \leq t < t_I \\ t_I, & \text{if } t \geq t_I. \end{cases}$$

$$k(s, u_L(s;\omega);\omega) = -\frac{c}{V^*}[u_L(s;\omega) - u(l,s-\gamma;\omega)],$$

and $u(l, s-\gamma;\omega) = 0$ if $s < \gamma$. Let the initial injection be given by

$$u_I(t) = \begin{cases} u^*, & 0 \leq t \leq t_I \\ 0, & \text{otherwise}. \end{cases}$$

For $0 \leq t < \gamma$, one can use the usual successive approximation method for deterministic integral equations of the Volterra type to show a solution exists, [13]. For $\gamma \leq t \leq M$, $\gamma < M < \infty$, we shall show that the stochastic integral equation (3.6) satisfies Theorem 3.1.

For $\omega \in \Omega$, the concentration $u_L(t;\omega)$ and $u(l,\ t-\gamma;\omega)$ can be considered as continuous functions of time, and hence $k(t, u_L(t;\omega);\omega)$ is continuous in t and u_L. For each t and u_L, $k(t, u_L;\omega)$ is a degenerate random variable (a constant). Hence for each t and u_L, $k(t,\ u_L;\omega) \in L_p(\Omega, A, \mu)$, $1 < p < \infty$, trivially, and so condition (*i*) of Theorem 2.1 is satisfied.

By the nature of the physical problem, the maximum value that $u_L(t;\omega)$ or $u(l,\ t-\gamma;\omega)$ can assume is u^*, and the minimum value is 0 for all $t \in [\gamma, M]$. Therefore,

$$\sup_{u_L} |k(t, u_L;\omega)| = \sup_{u_L}\left|\frac{c}{V^*}\,u_L(t;\omega) - u(l,t-\gamma;\omega)\right| = \frac{c}{V^*}\,u^*.$$

Let the degenerate random variable

$$g(\omega) = \frac{c\,u^*}{V^*},\ \omega \in \Omega.$$

Then $g(\omega) \in L_p(\Omega, A, \mu)$ because

$$\left\{\int_\Omega \left|g(\omega)\right|^p d\mu(\omega)\right\}^{\frac{1}{p}} = \frac{c\,u^*}{V^*} < \infty,$$

and condition (*ii*) of Theorem 3.1 is satisfied.

The stochastic free term $h(t;\omega)$ is the deterministic function $G(t)$ which is bounded.

$$|G(t)| \leq \int_0^{T(t)} \frac{c}{V^*}u_I(s)\,ds \leq \frac{t_I\,c\,u^*}{V^*} < \infty$$

for all $t \in [0, M]$. Hence $h(t;\omega) = G(t)$ μ-a.e. is in $L_p(\Omega,\ A, \mu)$, that is,

$$\left\{\int_\Omega \left|h(t;\ \omega)\right|^p d\mu(\omega)\right\}^{\frac{1}{p}} \leq \frac{t_I\,u^*c}{V^*} < \infty.$$

Since $G(t)$ is an integral, obviously, $h(t;\omega)$ is a continuous function from $[0,\ M]$ into $L_p(\Omega, A, \mu)$. Let $t \in [\gamma, M] < [0, M]$, $t_I < M < \infty$. Then

$$h(t;\omega)| + \int_0^t \sup_{u_L} |k(s, u_L; \omega)| \, ds$$

$$= \left| G(t) \right| + \int_0^t \frac{c\,u^*}{V^*} \, ds \leqslant t_l \frac{c\,u^*}{V^*} + t \frac{c\,u^*}{V^*}$$

$$\leqslant \frac{c\,u^*}{V^*}(t_l + M), \omega \quad \Omega.$$

Take

$$N_M = \left[\frac{c\,u^*}{V^*}(t_l + M) \right] + 1 < \infty,$$

where [.] is the greatest integer function. Then condition (*iii*) of Theorem 3.1 is satisfied.

Consider the sequence $\{u_{L,n}(t;\omega)\}$ which converges to $u_L(t;\omega)$ in $L_p(\Omega, A, \mu)$ for each $t \in [\gamma, M]$. Then for every $\varepsilon_1 > 0$ there exists an $N > 0$ such that whenever $n > N$,

$$\left\{ \int_\Omega \left| u_{L,n}(t;\omega) - u_L(t;\omega) \right|^p d\mu(\omega) \right\}^{\frac{1}{p}} < \varepsilon_1.$$

Therefore, letting $\varepsilon = c\,\varepsilon_1 / V^* > 0$, we have

$$\left\{ \int_\Omega \left| k(t, u_{L,n}(t;\omega);\ \omega) - k(t, u_L(t;\omega);\omega) \right|^p d\mu(\omega) \right\}^{\frac{1}{p}}$$

$$= \frac{c}{V^*} \left\{ \int_\Omega \left| u_{L,n}(t;\omega) - u_L(t;\omega) \right|^p d\mu(\omega) \right\}^{\frac{1}{p}} < \frac{c}{V^*}\varepsilon_1 = \varepsilon,$$

whenever $n > N$. That is, $k(t, u_{L,n}(t;\omega);\omega)$ converges to $k(t, u_L(t;\omega);\omega)$ in $L_p(\Omega, A, \mu)$. Since strong convergence implies weak convergence, condition (*iv*) of Theorem 3.1 is satisfied. Thus a random solution of Equation (3.6) exists for $t \in [\gamma, M]$.

Therefore, we have shown that the semi-stochastic integral equation (3.6) which represents the stochastic version of the chemotherapy model possesses a semi-random solution for $t \in [0, M]$, $0 < M < \infty$, $\gamma < M$ and $t_l < M$.

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ECUAȚII INTEGRALE STOCASTICE ÎN INGINERIE ȘI ȘTIINȚE BIOLOGICE

Rezumat

În modelele matematice ale fenomenelor din domeniul ingineriei, științelor biologice și fizice, apar frecvent ecuații stocastice [4], [10], [11]. Scopul articolului este de a formula metodele stocastice în mecanica fluidelor și chemoterapie, care conduc la ecuații integrale stocastice de forma (1.1), (1.2). Se ocupă de asemenea de existența unei soluții și de interpretarea ei fizică în metodele menționate mai sus.