MARTINGALE APPROACH FOR MODELING DNA SYNTHESIS

A. Gerardi - G. Nappo

Dip. di Matematica

Università di Roma "La Sapienza"

ABSTRACT

The relation between continuous and discrete models for DNA synthesis is treated. A law of large numbers is given when cells can die during the mitotic period. In the critical case the fluctuations around an equilibrium state are studied. In particular the convergence to an Ornstein-Uhlenbeck-type process is proved.

INTRODUCTION

The growth of a cell population in relation to the amount of DNA contained in each cell has been studied in the literature in two different kinds of models. (see (F.V.), (R.) and for a large survey (B.G.G.))

In a discrete models the DNA grows by finite quantities; in continuous models the behaviour of DNA growth is derived by hydrodynamic techniques.

In (G.N.) we connected discrete and continuous models in the sense of the weak convergence. More precisely we constructed a sequence of measure-valued discrete stochastic processes μ^k and proved a law of large numbers. We studied also some qualitative properties of the limit process μ and in particular we found an "equilibrium" state for it. We summarize these results in section 1.

In this paper, we consider the critical case: that is the case in which the total amount of particles is a martingale, and therefore its expectation is constant.

Our main purpose is to study the fluctuations around the equilibrium state. To this end we need an improvement of the result contained in (G.N). In section 2 one can find an estimate of the rate of convergence, obtained by a useful martingale representation of the approximating processes.

To study the convergence of fluctuations we use the classical technique: tightness, identification, uniqueness. (see sections 4, 5, 6)

As far as tightness is concerned, the main problem is the right choice of the state space: in order to find a solution the state space has to be sufficiently large, but not too much if you

want uniqueness. We choose a suitable nuclear space, suggested by Mitoma tightness criterion. (see (M.)) A detailed discussion on this subject can be found in section 3.

We prove then that the fluctuation approximating sequence ξ^k converges to an Ornstein-Uhlenbeck-type process ξ associated to the operator A defined in (3.2). We want to point out that the main technical tool for the identification is the estimate of the rate of convergence, given in section 2.

Note that in the limit process ξ the "diffusion term" (D.) degenerates. This is related to the peculiarity of the branching mechanism: the daughter-cells are born in a state different from the mother-cell state. To clarify this remark we describe heuristically the mathematical model of DNA synthesis. Every cell of a given population has the same behaviour: it produces DNA with a given synthesis velocity $v(\cdot)$ until it doubles the initial amount. Afterwards there is a gap period and mitosis. This time interval is exponentially distributed with rate $\lambda_1 > 0$ and during it the quantity of DNA remains constant. At the end of this period the cell can split into two identical cells, with probability α , or it can die with probability $1 - \alpha$. Every daughter cell waits for a second exponentially distributed gap period (of parameter $\lambda_0 > 0$) and then the cycle starts anew. Moreover we assume that each cell moves independently of each other.

In the discrete description, when the DNA content increases by a finite quantity $1/k$, every cell moves in the set $X_k = \{G\} \cup \{i/k, i=0, \dots, k\}$ where G represents the second gap period, $x=0$ represents the initial amount of DNA and $x=1$ the final one. The cell stays in $x=i/k$ ($i=0, \dots, k-1$) an exponential time of parameter $kv(x)$, and then it jumps to the next point $x + 1/k$. In G and in $x=1$ the parameters are λ_0, λ_1 respectively. For every $x \in X_k$,

4.

$\mu_t^k(x)$ is the number of cells in the state x at time t , scaled by the factor $\epsilon(k)$.

As a final remark observe that the $\epsilon(k)$ is chosen by considering the behaviour of the initial distribution. Indeed we assume that the initial number of cells increases to infinity, and $\epsilon(k)$ is a normalizing factor, such that the sequence μ_o^k converges.

§ 1. LAW OF LARGE NUMBERS

Let

$$X = [0,1] \cup \{G\}$$

and for every k

$$X_k = \{\frac{i}{k}, i=0, \dots, k\} \cup \{G\}$$

Let M denote the space of non negative Radon measures on X with the topology of the weak convergence and M_k the subspace of the purely atomic measures with atoms in X_k .

Let $v(x)$ be a real valued continuous function on X such that $0 < v \leq v(x) \leq V$.

The microscopic processes we are interested in, are defined as the solution of the martingale problem (MGP) associated to the following operator:

$$\begin{aligned} L_k f(\mu) = & \sum_{i=0}^{k-1} k \epsilon(k) v\left(\frac{i}{k}\right) \mu\left(\frac{i}{k}\right) \left[f\left(\mu + \frac{\delta_{\frac{i+1}{k}} - \delta_{\frac{i}{k}}}{\epsilon(k)}\right) - f(\mu) \right] \\ & + \lambda_o \epsilon(k) \mu(G) \left[f\left(\mu + \frac{\delta_o - \delta_G}{\epsilon(k)}\right) - f(\mu) \right] + \end{aligned} \quad (1.1)$$

$$\begin{aligned}
& + \lambda_1 (1-\alpha) \varepsilon(k) \mu(1) \left[f\left(\mu - \frac{\delta_1}{\varepsilon(k)}\right) - f(\mu) \right] + \\
& + \lambda_1 \alpha \varepsilon(k) \mu(1) \left[f\left(\mu + \frac{2\delta_G - \delta_1}{\varepsilon(k)}\right) - f(\mu) \right]
\end{aligned}$$

for $f \in C_b(M_k)$.

It is well known that the solution of the MGP associated to L_k exists and is unique for every initial condition $\mu_0^k \in M_k$ as a consequence of linearity of the jump rates. (E.K., chp. 4.11)

Furthermore, (E.K.) by a random time change technique the solution can be represented in a fixed probability space $(\Omega, \mathcal{F}, (\mathcal{F}_t), P)$ as

$$\begin{aligned}
\mu_t^k = & \frac{1}{\varepsilon(k)} \left[\sum_{i=0}^{k-1} \left(\frac{\delta_{i+1}}{k} - \frac{\delta_i}{k} \right) N_i^k \left(k \varepsilon(k) \nu\left(\frac{1}{k}\right) \int_0^t \mu_s^k \left(\frac{1}{k}\right) ds \right) + \right. \\
& + (\delta_0 - \delta_G) N_{-1}^k (\lambda_0 \varepsilon(k) \int_0^t \mu_s^k(G) ds) + \\
& - \delta_1 N_k^k ((1-\alpha) \lambda_1 \varepsilon(k) \int_0^t \mu_s^k(1) ds) + \\
& \left. + (2\delta_G - \delta_1) N_{k+1}^k (\alpha \lambda_1 \varepsilon(k) \int_0^t \mu_s^k(1) ds) \right] + \mu_0^k.
\end{aligned} \tag{1.2}$$

Here, for $\ell = -1, 0, \dots, k+1$, N_ℓ^k are independent standard Poisson processes.

The limit process is deterministic and it can be characterized as the unique solution of the MGP for the operator

$$L_f(\mu) = \nabla F(\langle \mu, \phi \rangle) \langle \mu, B\phi \rangle^{(.)} \tag{1.3}$$

$$(.) \quad \langle \mu, \phi \rangle = \int_X \phi(x) \mu(dx).$$

on functions $f(\mu) = F(\langle \mu, \phi \rangle)$ such that

$$(i) \quad F \in C_c^1(\mathbb{R}),$$

$$(ii) \quad \phi \text{ bounded on } X \text{ and } C^1 \text{ in } [0,1]$$

$$(iii) \quad B\phi(\cdot) \text{ continuous on } X.$$

where

$$\begin{aligned} B\phi(G) &= \lambda [\phi(0) - \phi(G)] \\ B\phi(x) &= v(x) \phi'(x) & x \in [0,1] \\ B\phi(1) &= \lambda_1 [2\alpha\phi(G) - \phi(1)] \end{aligned} \tag{1.4}$$

In the sequel we will call $\mathcal{D}$ the set of the functions f satisfying (i), (ii), (iii) and $\mathcal{D}_B$ the set of the functions ϕ satisfying (ii) and (iii). The choice of the operator L is not surprising: the formal limit of $L_k f(\mu)$ is $Lf(\mu)$ if $f(\mu) = F(\langle \mu, \phi \rangle)$. Observe that the MGP associated to the operator L is well posed. The existence follows by the fact that B generates a positive preserving and strongly continuous semigroup e^{tB} on $C_b(X)$: a solution is the process μ_t defined by

$$\langle \mu_t, \phi \rangle = \langle \mu_0, e^{tB} \phi \rangle \quad \phi \in C_b(X) \tag{1.5}$$

The uniqueness can be proved by a duality argument (G.N., § 3).

In this setting we can state the main result related to the law of large numbers.

Theorem 1

The sequence $\{\mu_t^k\}$ defined by (1.2) converges in law to the process μ_t defined in (1.5) in $D_M[0, T]$ if $\{\mu_o^k\}$ converges in law to μ_o in M and $\{E \|\mu_o^k\|_{BV}\}$ is uniformly bounded.

Classical branching techniques cannot be applied in this case since the daughter cells are born in a state different from the one in which the mother dies. So, to prove the theorem, we use a general convergence criterion, stated in the following proposition, which is a suitable formulation of some results on approximations (E.K.).

Proposition

Let S be a complete separable metric space, $S_k \subset S$, and for any $f \in C(S)$ let $\pi_k f := f|_{S_k}$.

Let X_k be a solution of the MGP for $(A_k, \mathcal{L}(X_k(0)))$ in $D_{S_k}[0, T]$, where $\mathcal{L}(X_k(0))$ is the law of $X_k(0)$.

Let A be an operator with domain $D_A \subseteq C(S)$, such that the MGP associated to $(A, \mathcal{L}(X(0)))$ has at most one solution and the linear span generated by D_A contains an algebra separating points.

If

1. $\forall \epsilon > 0, \exists$ a compact set $K \subseteq S$ such that

$$\inf_k P(X_k(t) \in K, \forall t \in [0, T]) \geq 1 - \epsilon.$$
2. There exists $G_k \subseteq S_k$:

$$\lim_{k \rightarrow \infty} P(X_k(t) \in G_k, \forall t \in [0, T]) = 1$$
3. For any $f \in D_A$, $\pi_k f$ is in the domain of A_k and

$$\lim_{k \rightarrow \infty} \sup_{G_k} |\pi_k(Af) - A_k(\pi_k f)| = 0$$

4. $X_k(0)$ converges in law to $X(0)$ in S .

Then the MGP for $(A, \mathcal{L}(X(0)))$ has a solution and the sequence X_k converges in distribution to X in $D_S[0, T]$.

Proof of Theorem 1:

Thanks to (1.2) the bounded variation norm: $\|\mu_t^k\|_{B.V.} = \mu_t^k(X)$ is a super(sub)-martingale when $\alpha \leq 1/2$ ($\alpha \geq 1/2$).

Then

$$\begin{aligned} P\left(\sup_{t \in [0, T]} \|\mu_t^k\|_{B.V.} \geq \Delta\right) &\leq \frac{1}{\Delta} \sup_{t \in [0, T]} E \|\mu_t^k\|_{B.V.} \leq \\ &\leq \frac{1}{\Delta} E \|\mu_0^k\| \exp(|2\alpha-1|\lambda_1 T). \end{aligned}$$

Moreover, by a direct computation, if $\pi_k f := f|_{M_k}$, $f \in \mathcal{D}$ one can obtain that

$$|Lf(\mu) - L_k(\pi_k f)(\mu)| \leq \|\mu\|_{B.V.} O\left(\frac{1}{k}\right).$$

Let $\{\Delta_k\}$ be a diverging sequence satisfying

$$\lim_{k \rightarrow \infty} \frac{\Delta_k}{k} = 0$$

and let

$$G_k = \{\mu \in M_k : \|\mu\|_{B.V.} \leq \Delta_k\}$$

then one has

$$\lim_{k \rightarrow \infty} P(\mu_t^k \in G_k, \forall t \in [0, T]) = 1$$

$$\lim_{k \rightarrow \infty} \sup_{\mu \in G_k} |Lf(\mu) - L_k(\pi_k f)(\mu)| = 0.$$

Since $\mathcal{D}$ is an algebra separating points, this in turn implies that μ^k converges to μ .

§ 2. LAW OF LARGE NUMBERS: CRITICAL CASE

We recall that from now on we will assume $\alpha = 1/2$. In this case we observe that the approximating processes have an "equilibrium" point, in the sense that, for every k , we can find a measure $\hat{\mu}^k \in M_k$, such that, for every function ϕ on X

$$E \langle \mu_t^k, \phi \rangle = \langle \hat{\mu}^k, \phi \rangle \quad (2.1)$$

if $E \mu_o^k = \hat{\mu}^k$. More precisely

Lemma 1

The measure $\hat{\mu}^k$ in (2.1) is the solution, unique up to a multiplicative factor, of the equation

$$\langle \hat{\mu}^k, B_k \phi \rangle = 0 \quad (2.2)$$

where

$$\begin{aligned} B_k \phi(G) &= B \phi(G) = \lambda_o [\phi(0) - \phi(G)] \\ B_k \phi(i/k) &= kv(i/k) [\phi(\frac{i+1}{k}) - \phi(\frac{i}{k})] \quad i = 0, \dots, k-1. \\ B_k \phi(1) &= B \phi(1) = \lambda_1 [\phi(G) - \phi(1)] \end{aligned}$$

Thus, for each k , $\hat{\mu}^k$ has the role of an equilibrium state around

which μ_t^k fluctuates. Note that $\hat{\mu}^k$ is defined up to a multiplicative factor. If we take the particular solution $\hat{\mu}^k$ defined by

$$\begin{aligned}\hat{\mu}^k(G) &= 1/\lambda_0 \\ \hat{\mu}^k(i/k) &= 1/kv(i/k) \quad i = 0, \dots, k-1 \\ \hat{\mu}(1) &= 1/\lambda_1\end{aligned}$$

the sequence $\{\hat{\mu}^k\}$ converges weakly to a measure $\hat{\mu} \in M$:

$$\hat{\mu}(dx) = \frac{1}{v(x)} dx + \frac{1}{\lambda_0} \delta_G(dx) + \frac{1}{\lambda_1} \delta_1(dx) \quad (2.3)$$

It is easy to see that $\hat{\mu}$ verifies

$$\langle \hat{\mu}, B\phi \rangle = 0, \quad \forall \phi \in D_B \quad (2.4)$$

and taking into account (1.5), (2.4) is equivalent to

$$\langle \mu_t, \phi \rangle = \langle \hat{\mu}, \phi \rangle$$

if $\mu_0 = \hat{\mu}$. (G.N.)

Our aim is to study the limit of the fluctuations of μ_t^k around its mean value. We start by an estimate of the variance of the approximating process evaluated on a suitable class of functions.

Lemma 2

For every $\phi \in C(X)$ and C^1 in $[0,1]$

$$\sigma^2(\langle \hat{\mu}_t^k, \phi \rangle) \leq \frac{Ct}{\epsilon(k)} \left(\sup_x |\phi|^2 + \sup_{[0,1]} |\phi'|^2 \right) \hat{\mu}^k(X)$$

where C is a positive constant.

This lemma is fundamental for finding the right scaling of the fluctuations. To prove the convergence, in particular to identify the limit, we will need an improvement of this result which is stated in the following

Theorem 2

If $\mu_o^k = \hat{\mu}^k$, then

$$\sup_{t \in [0, T]} \sum_{x \in X_k} \sigma^2(\mu_t^k(x)) = O\left(\frac{1}{\varepsilon(k)}\right) \quad (2.5)$$

We end this section by giving the proofs of the lemmas and of the theorem.

Proof of Lemma 1

Note that (2.2) is equivalent to

$$\langle \hat{\mu}^k, e^{tB_k(\pi_k \phi)} \rangle = \text{const.}$$

For the thesis we need a further representation for μ_t^k .

Let us set:

$$\begin{aligned} Y_{-1}^k(t) &= N_{-1}^k(\lambda_o \varepsilon(k) \int_o^t \mu_s^k(G) ds) - \lambda_o \varepsilon(k) \int_o^t \mu_s^k(G) ds \\ Y_\ell^k(t) &= N_\ell^k(k \varepsilon(k) v(i/k) \int_o^t \mu_s^k(i/k) ds) - \\ &\quad - k \varepsilon(k) v(i/k) \int_o^t \mu_s^k(i/k) ds \quad \ell = 0, \dots, k-1 \end{aligned} \quad (2.6)$$

$$\begin{aligned} Y_\ell^k(t) &= N_\ell^k(1/2 \lambda_1 \varepsilon(k) \int_o^t \mu_s^k(1) ds) - 1/2 \lambda_1 \varepsilon(k) \int_o^t \mu_s^k(1) ds \\ &\quad \ell = k, k+1 \end{aligned}$$

we observe that $\{Y_\ell^k\}$ is a family of zero-mean orthogonal martingales, (E.K.), such that

$$\begin{aligned} \langle\langle Y_{-1}^k \rangle\rangle_t &= \lambda_0 \epsilon(k) \int_0^t \mu_s^k(G) ds \\ \langle\langle Y_\ell^k \rangle\rangle_t &= k \epsilon(k) v(i/k) \int_0^t \mu_s^k(i/k) ds \quad \ell = 0, \dots, k-1 \\ \langle\langle Y_\ell^k \rangle\rangle_t &= 1/2 \lambda_1 \epsilon(k) \int_0^t \mu_s^k(1) ds \quad \ell = k, k+1 \end{aligned} \quad (2.7)$$

where $\langle\langle \cdot \rangle\rangle$ is the predictable quadratic variation of a martingale.

From (1.2) we get

$$\begin{aligned} \langle \mu_t^k, \phi \rangle &= \langle \mu_0^k, \phi \rangle + \int_0^t \langle \mu_s^k, B_k \phi \rangle ds + \\ &+ \frac{\phi(0) - \phi(G)}{\epsilon(k)} Y_{-1}^k(t) + \sum_{\ell=0}^{k-1} \frac{\phi(\frac{\ell+1}{k}) - \phi(\frac{\ell}{k})}{\epsilon(k)} Y_\ell^k(t) - \\ &- \frac{\phi(1)}{\epsilon(k)} Y_k^k(t) + \frac{2\phi(G) - \phi(1)}{\epsilon(k)} Y_{k+1}^k(t) = \\ &= \langle \mu_0^k, \phi \rangle + \int_0^t \langle \mu_s^k, B_k \phi \rangle ds + \langle z_t^k, \phi \rangle \end{aligned} \quad (2.8)$$

where the definition of the martingale z_t^k is implicit.

It follows immediately that:

$$\langle \mu_t^k, \phi \rangle = \langle \mu_0^k, e^{tB_k}(\pi_k \phi) \rangle + \int_0^t \langle dz_s^k, e^{(t-s)B_k}(\pi_k \phi) \rangle \quad (2.9)$$

From (2.9)

$$\langle E \mu_t^k, \phi \rangle = \langle E \mu_0^k, e^{tB_k}(\pi_k \phi) \rangle$$

If $E \mu_o^k = \hat{\mu}^k$, the thesis follows.

Proof of Lemma 2

By using the representation (2.9) with $\mu_o^k = \hat{\mu}^k$, we have that

$$E | \langle \mu_t^k, \phi \rangle - \langle \hat{\mu}^k, \phi \rangle |^2 = E | \int_o^t \langle dz_s^k, e^{(t-s)B_k(\pi_k \phi)} \rangle |^2$$

The estimate is based, as previously, on the (2.1), (2.7) and on the following remark:

$$\begin{aligned} & [e^{(t-s)B_k(\pi_k \phi)(\frac{i+1}{k})} - e^{(t-s)B_k(\pi_k \phi)(i/k)}] k v(i/k) = \\ & = B_k(e^{(t-s)B_k(B_k \phi)})(i/k) = \\ & = e^{(t-s)B_k(B_k \phi)}(i/k) . \end{aligned}$$

$$|e^{(t-s)B_k(B_k \phi)}(i/k)| \leq C_2 (\sup_x |\phi| + \sup_{[0,1]} |\phi'|) .$$

Proof of the theorem

We start with $x = G$. From Lemma 2 by choosing $\phi = I_{\{G\}}$, we get

$$\sigma^2(\mu_t^k(G)) \leq \frac{Ct}{\varepsilon(k)} \quad (2.10)$$

Now let $x = 0$. From (2.8) with $\phi = I_{\{0\}}$

$$\begin{aligned} \mu_t^k(0) - \hat{\mu}^k(0) &= -kv(0) \int_o^t [\mu_s^k(0) - \hat{\mu}^k(0)] ds + \\ &+ \lambda_o \int_o^t [\mu_s^k(G) - \hat{\mu}^k(G)] ds + \frac{1}{\varepsilon(k)} [Y_{-1}^k(t) - Y_o^k(t)] \end{aligned}$$

$$\begin{aligned}
\mu_t^k\left(\frac{i}{k}\right) - \hat{\mu}^k\left(\frac{i}{k}\right) &= -kv\left(\frac{i}{k}\right) \int_0^t [\mu_s^k\left(\frac{i}{k}\right) - \hat{\mu}^k\left(\frac{i}{k}\right)] ds + \\
&+ kv\left(\frac{i-1}{k}\right) \int_0^t [\mu_s^k\left(\frac{i-1}{k}\right) - \hat{\mu}^k\left(\frac{i-1}{k}\right)] ds + \\
&+ \frac{1}{\varepsilon(k)} [Y_{i-1}^k(t) - Y_i^k(t)] .
\end{aligned}$$

And finally for $x = 1$

$$\begin{aligned}
\mu_t^k(1) - \hat{\mu}^k(1) &= -\lambda_1 \int_0^t [\mu_s^k(1) - \hat{\mu}^k(1)] ds + \\
&+ kv\left(\frac{k-1}{k}\right) \int_0^t [\mu_s^k\left(\frac{k-1}{k}\right) - \hat{\mu}^k\left(\frac{k-1}{k}\right)] ds + \\
&+ \frac{1}{\varepsilon(k)} [Y_{k-1}^k(t) - Y_{k+1}^k(t) + Y_k^k(t)] .
\end{aligned}$$

This system is linear and can be solved recursively, as a function of $\mu_t^k(G) - \hat{\mu}^k(G)$. The solution is:

$$\begin{aligned}
\mu_t^k\left(\frac{i}{k}\right) - \hat{\mu}^k\left(\frac{i}{k}\right) &= \\
&= \frac{1}{v(i/k)} e^{-kv(i/k)t} \{k^i \prod_{\ell=0}^{i-1} v(\ell/k) \int_0^t F_0^i(t,u) \lambda_0 [\mu_u^k(G) - \hat{\mu}^k(G)] du \\
&+ \frac{1}{\varepsilon(k)} \sum_{j=0}^{i-1} k^{i-j} \prod_{\ell=j}^{i-1} v(\ell/k) \int_0^t F_j^i(t,u) d[Y_{i-1}^k(u) - Y_i^k(u)] \}
\end{aligned}$$

for $i = 0, \dots, k-1$.

and

$$\begin{aligned}
\mu_t^k(1) - \hat{\mu}^k(1) &= k^k \prod_{\ell=0}^{k-1} v(\ell/k) e^{-\lambda_1 t} \int_0^t e^{\lambda_1 s - kv\left(\frac{k-1}{k}\right)s} \int_0^s F_0^{k-1}(s,u) \cdot \\
&\cdot \lambda_0 [\mu_u^k(G) - \hat{\mu}^k(G)] du ds +
\end{aligned}$$

$$\begin{aligned}
& + \frac{e^{-\lambda_1 t}}{\varepsilon(k)} \left\{ \sum_{j=0}^{k-1} k^{k-j} \prod_{\ell=j}^{k-1} v(\ell/k) \int_0^t \int_u^t e^{\lambda_1 s - kv(\frac{k-1}{k})s} \right. \\
& \cdot F_j^{k-1}(s, u) ds \, d[Y_{j-1}^k(u) - Y_j^k(u)] + \\
& \left. + \int_0^t e^{\lambda_1 u} \, d[Y_{k-1}^k(u) - Y_{k+1}^k(u) + Y_k^k(u)] \right\}
\end{aligned}$$

where, $\forall i$

$$\begin{aligned}
F_j^i(t, u) &= \int_u^t e^{k[v(i/k) - v(\frac{i-1}{k})]s} F_j^{i-1}(s, u) \, ds \\
&\quad j = 0, \dots, i-1 \\
F_i^i(t, u) &= e^{kv(i/k)u}
\end{aligned}$$

By using these expressions we obtain:

$$E \left| \mu_t^k\left(\frac{i}{k}\right) - \hat{\mu}\left(\frac{i}{k}\right) \right|^2 \leq C_1 t/k \varepsilon(k)$$

$$E \left| \mu_t^k(1) - \hat{\mu}(1) \right|^2 \leq C_2 t/\varepsilon(k)$$

and then the thesis. The two estimates above are based on the fact that the martingales $Y_\ell^k(t)$ are orthogonal and their quadratic variation (see (2.7) and (2.1)) has expectation

$$E \ll Y^k \gg_t = t \varepsilon(k) \quad \ell = -1, \dots, k$$

and moreover on (2.10) and the following technical properties:

1.
$$\int_0^t F_0^i(t, u) du \leq \frac{e^{kv(i/k)t}}{k^{i+1} \prod_{\ell=0}^i v(\ell/k)}$$
2.
$$\frac{\partial}{\partial u} F_j^i(t, u) = kv(j/k) F_j^i(t, u) - F_{j+1}^i(t, u) \quad i \geq 1 ; j=0, \dots, i-1$$

which can be proved by induction.

§ 3. CENTRAL LIMIT THEOREM: MAIN TOOLS

We start to study the fluctuations of μ_t^k around the mean value $\hat{\mu}^k$, under the condition $\mu_o^k = \hat{\mu}^k$. The right scaling, as suggested by Lemma 2, is the classical one:

$$\xi_t^k = \sqrt{\varepsilon(k)} (\mu_t^k - \hat{\mu}^k)$$

We want to study the convergence of the sequence $\{\xi_t^k\}$. The first step is the computation of the operator A_k associated to the process ξ_t^k . On the functions $f(\cdot) = F(\langle \cdot, \phi \rangle)$ the form of A_k can be easily deduced from (1.1):

$$\begin{aligned} A_k f(\xi) &= \sum_{i=0}^{k-1} k \sqrt{\varepsilon(k)} v(i/k) [\xi(i/k) + \sqrt{\varepsilon(k)} \hat{\mu}^k(i/k)] \cdot \\ &\cdot [F(\langle \xi, \phi \rangle + \frac{\phi((i+1)/k) - \phi(i/k)}{\sqrt{\varepsilon(k)}}) - F(\langle \xi, \phi \rangle)] + \\ &+ \lambda_o \varepsilon(k) [\xi(G) + \sqrt{\varepsilon(k)} \hat{\mu}^k(G)] [F(\langle \xi, \phi \rangle + \frac{\phi(0) - \phi(G)}{\sqrt{\varepsilon(k)}}) - F(\langle \xi, \phi \rangle)] \\ &+ \frac{1}{2} \lambda_1 \sqrt{\varepsilon(k)} [\xi(1) + \sqrt{\varepsilon(k)} \hat{\mu}^k(G)] [F(\langle \xi, \phi \rangle - \frac{\phi(1)}{\sqrt{\varepsilon(k)}}) + \\ &+ F(\langle \xi, \phi \rangle + \frac{2\phi(G) - \phi(1)}{\sqrt{\varepsilon(k)}}) - 2F(\langle \xi, \phi \rangle)] . \end{aligned}$$

Taking the formal limit of (3.1), for $\phi \in D_B$, one obtains the following operator

$$\begin{aligned}
\Lambda f(\xi) &= F'(\langle \xi, \phi \rangle) \langle \xi, B \phi \rangle + \\
&+ \frac{1}{2} \sum_{i,j=-1,0,1} q_{ij} \phi(i) \phi(j) F''(\langle \xi, \phi \rangle)
\end{aligned}
\tag{3.2}$$

where, for notational convenience, we identify G with -1 and

$$\| q_{ij} \| = \left\| \begin{pmatrix} 3 & -1 & -1 \\ -1 & 1 & 0 \\ -1 & 0 & 1 \end{pmatrix} \right\| \quad i,j=-1,0,1$$

So one expects that the limit law is the solution of the MGP associated to (3.2) in a suitable space E' and for a suitable class $\mathcal{D}_A$ of functions f .

More precisely, what we have to do is to prove the tightness of the sequence in $D_{E'}[0,T]$. The convergence then follows, once we identify the limit law and prove the uniqueness of the MGP associated to A in the same space. The choice of E' is suggested by Mitoma tightness criterion. Roughly speaking, if E' is the topological dual of a nuclear Fréchet space E , and if $\{\eta_t^k\}$ is a sequence of E' -valued stochastic processes, this criterion allows to prove the tightness of $\{\eta_t^k\}$ by the tightness of the sequence of real-valued-processes $\langle \eta_t^k, \phi \rangle$, for every fixed $\phi \in E$, (M.). Therefore it enables to apply classical criterion for real-valued processes.

These considerations, and the construction of the operator A , lead to the following choice:

Lemma 3

The space $E = \{\phi \in \mathcal{D}_B, \text{ such that } \phi \text{ is } C^\infty \text{ in } [0,1]\}$ is a nuclear Fréchet space.

Proof

The topology in E is defined by the seminorms

$$\|\phi\|_0^E = |\phi(G)| + \left[\int_0^1 |\phi(x)|^2 dx \right]^{\frac{1}{2}}$$

$$\|\phi\|_p^E = \|\phi\|_{p-1}^E + \left[\int_0^1 \left| \frac{d^p}{dx^p} \phi(x) \right|^2 dx \right]^{\frac{1}{2}}$$

Then the thesis follows observing that the map

$$\phi \in E \rightarrow \phi|_{[0,1]} \in C^\infty[0,1]$$

is an isomorphism between E and $C^\infty[0,1]$ endowed with the structure of nuclear space, defined by the seminorms $\|\phi\|_{W^{2,p}[0,1]}$. Indeed, every $\phi \in C^\infty[0,1]$, has a unique extension to a function belonging to $\mathcal{D}_B$.

We need a last remark: as a consequence of the choice of the space E , in order to make precise the meaning of the (3.2), we have to assume that $v(\cdot) \in C^\infty[0,1]$. Note that the symbol $\langle \cdot, \cdot \rangle$ from now on represents the duality relation between E' and E .

§ 4. CENTRAL LIMIT THEOREM: TIGHTNESS

Thanks to Mitoma criterion (M.), the tightness of $\{\xi^k\}$ in $\mathcal{D}_E[0,T]$ is equivalent to the following theorem:

Theorem 3

The real-valued processes $\langle \xi_t^k, \phi \rangle$ are tight in $\mathcal{D}_R[0,T]$ for every $\phi \in E$.

Proof

As proved in (E.k), tightness is implied by the following conditions

$$(a) \quad \forall t, \forall \phi \in E, \exists C > 0 : E[|\langle \xi_t^k, \phi \rangle|^2] \leq C \quad \forall k.$$

(b) $\forall t, \forall \phi \in E, \forall \delta > 0, \forall k$ there exists a random variable $\gamma^k(\delta)$ such that

$$E[|\langle \xi_{t+u}^k, \phi \rangle - \langle \xi_t^k, \phi \rangle|^2 | \mathcal{F}_t] \leq E[\gamma^k(\delta) | \mathcal{F}_t] \quad \forall u \leq \delta$$

$$\lim_{\delta \rightarrow 0} \sup_k E[\gamma^k(\delta)] = 0$$

Relation (a) is an immediate consequence of lemma 2. As far as (b) is concerned, by a direct computation, and taking into account the representation (2.9), one has:

$$\begin{aligned} & |\langle \xi_{t+u}^k, \phi \rangle - \langle \xi_t^k, \phi \rangle|^2 \leq \\ & \leq \frac{2}{\epsilon(k)} \cdot \{ |\int_0^t \langle dz_s^k, \int_{t-s}^{t+u-s} e^{\sigma B_k(B_k \phi)} d\sigma |^2 + \\ & + |\int_t^{t+u} \langle dz_s^k, e^{(t+u-s)B_k(\pi_k \phi)} \rangle|^2 \} \end{aligned}$$

By using the same idea as in Lemma 2 and the martingale property of $\mu_t^k(X)$, the conditional expectation of the first term is less or equal to

$$\begin{aligned} & 2C(\sup_X |\phi|^2 + \sup_{[0,1]} |\phi'|^2) E[\int_t^{t+u} \mu_s^k(X) ds | \mathcal{F}_t] \leq \\ & \leq C_2(\|\phi\|_2^E)^2 \mu_t^k(X) \delta. \end{aligned}$$

The second term, analogously, is less or equal to

$$\begin{aligned} & u^2 C_3 \left(\sup_k |B_k \phi|^2 + \sup_k |B_k^2 \phi|^2 \right) E \left[\int_0^t \mu_s^k(X) ds | \mathcal{F}_t \right] \leq \\ & \leq C_4 \delta^2 \left(\|\phi\|_3^E \right)^2 \int_0^t \mu_s^k(X) ds \end{aligned}$$

and the thesis follows since

$$\sup_k E \mu_s^k(X) = \sup_k \hat{\mu}^k(X) < +\infty.$$

Remark

Let $\{\xi_t^{k_n}\}$ be a subsequence of $\{\xi_t^k\}$ converging to ξ_t . For every $\phi \in E$, $\langle \xi_t^{k_n}, \phi \rangle$ converges to $\langle \xi_t, \phi \rangle$. Note that this process has continuous paths, because the jumps size of $\langle \xi_t^k, \phi \rangle$ goes to zero as $1/\sqrt{\epsilon(k)}$.

This remark will be useful in proving the convergence.

§ 5. CENTRAL LIMIT THEOREM: IDENTIFICATION

Let $\{\xi_t^{k_n}\}$ be a converging subsequence of $\{\xi_t^k\}$. We want to show that any limit point Q of the laws Q_{k_n} of $\xi_t^{k_n}$, is a solution of the MGP for A defined by (3.2) on the set

$$\mathcal{D}_A = \{f(\cdot) = F(\langle \cdot, \phi \rangle) : \phi \in E, B \phi \in E, F \in C_b^3(\mathbb{R})\}$$

Setting

$$H(\omega) := f(\omega(t)) - f(\omega(t_0)) - \int_{t_0}^t A f(\omega(s)) ds$$

this is equivalent to prove that for any $f \in D_A$ and any $t_0 \leq t \leq T$

$$E^Q[g(\omega) H(\omega)] = 0 \quad (5.1)$$

$\forall g \in C_b(D_E, [0, T])$ $\mathcal{G}_{t_0}$ -measurable, where $\{\mathcal{G}_t\}$ is the canonical filtration and $\omega(\cdot)$ is the canonical process in $D_E, [0, T]$.

It is natural to try to obtain (5.1) by the following relations:

$$\lim_{n \rightarrow \infty} E^{Q_{k_n}}[g(\omega) H(\omega)] = E^Q[g(\omega) H(\omega)] \quad (5.2)$$

$$\lim_{n \rightarrow \infty} E^{Q_{k_n}}[g(\omega) H(\omega)] = 0 \quad (5.3)$$

Unfortunately (5.2) is not a consequence of the convergence of Q_{k_n} , since $H(\omega)$ is neither continuous nor bounded. The continuity problem is solved by the remark in § 4. Indeed we need only that the set of discontinuity points of H has zero Q -measure, for any limit point Q , and H is continuous in ω if $\langle \omega(t), \phi \rangle$ is a continuous function. To circumvent the boundedness problem, we have to introduce a truncation technique. Namely we put

$$H_N := \begin{cases} -N & H < -N \\ H & |H| \leq N \\ N & H > N \end{cases}$$

Moreover let

$$H^k(\omega) := f(\omega(t)) - f(\omega(t_0)) - \int_{t_0}^t A_k f(\omega(s)) ds$$

Note that this is the same expression of $H(\omega)$ with Λ_k instead of A .

Theorem 4

Every limit point Q of $\{Q_k\}$ is a solution of the MGP associated to A on ∂_A .

Proof

The following relations imply (5.1) and then the thesis:

$$E^Q[gH] = \lim_{N \rightarrow \infty} E^Q[H_N g] \quad (5.4)$$

$$\lim_{N \rightarrow \infty} \lim_{k_n \rightarrow \infty} E^{Q_{k_n}}[H_N g] = 0 \quad (5.5)$$

since

$$E^Q[H_N g] = \lim_{k_n \rightarrow \infty} E^{Q_{k_n}}[H_N g]$$

H_N being bounded.

On the other hand $E^{Q_k}[H^k g] = 0$ and therefore

$$\lim_{N \rightarrow \infty} \lim_{k_n \rightarrow \infty} E^{Q_{k_n}}[(H_N - H)g] = 0 \quad (5.6)$$

$$\lim_{k_n \rightarrow \infty} E^{Q_{k_n}}[(H - H^{k_n})g] = 0 \quad (5.7)$$

are sufficient to prove (5.5).

Both (5.4) and (5.5) are consequence of the uniform integrability of H_N and H (remember that g is bounded).

To accomplish the thesis it remains to prove the following Lemmas.

Lemma 4

The random variables $H(\xi^k)$ and $H_N(\xi^k)$ are uniformly integrable, for every N , with respect to k .

Proof

The thesis is implied by $\sup E^{Q_k}[H^2] < +\infty$. Since the function F involved in the definition of H is bounded it is sufficient to prove that

$$\sup_k E^{Q_k} \left[\left| \int_{t_0}^t F'(\langle \omega(s), \phi \rangle) \langle \omega(s), B\phi \rangle ds \right|^2 \right] < +\infty$$

But

$$\begin{aligned} \left| \int_{t_0}^t F'(\langle \omega(s), \phi \rangle) \langle \omega(s), B\phi \rangle ds \right|^2 &\leq |t-t_0| \sup_{x \in \mathbb{R}} |F'(x)|^2 \\ &\quad \int_{t_0}^t |\langle \omega(s), B\phi \rangle|^2 ds \end{aligned}$$

Taking the expectation, the thesis follows from Lemma 2 since $B\phi \in E$, and $|H_N| \leq |H|$.

Lemma 5

For any $f \in \mathcal{D}_A$,

$$\lim_{k \rightarrow \infty} E^{Q_k} \left[\left| \int_{t_0}^t (AF(\langle \omega(s), \phi \rangle) - A_k F(\langle \omega(s), \phi \rangle)) ds \right| \right] = 0$$

which implies (5.7).

Proof

By a direct computation

$$\begin{aligned}
& E^Q_k \left[\left| \int_{t_0}^t (A^F(\langle \omega(s), \phi \rangle) - A_k^F(\langle \omega(s), \phi \rangle)) ds \right| \right] \leq \\
& \leq \text{const.} \{ E \left[\int_{t_0}^t |\sqrt{\epsilon(k)} \langle \mu_s^k, B_k \phi \rangle - \langle \xi_s^k, B \phi \rangle| + \right. \\
& + \frac{1}{k} (\|\phi\|_2^E)^2 \int_{t_0}^t \mu_s^k(X) ds + (|2\phi(G) - \phi(1)|^2 + |\phi(1)|^2) \int_0^t |\mu_s^k(1) - \hat{\mu}^k(1)| ds + \\
& \left. + |\phi(0) - \phi(G)|^2 \int_0^t |\mu_s^k(G) - \hat{\mu}^k(G)| ds + \frac{1}{\sqrt{\epsilon(k)}} (\|\phi\|_2^E)^3 \int_0^t \mu_s^k(X) ds \right] \}
\end{aligned}$$

where the constant depends on F , $v(\cdot)$, λ_0 , λ_1 . Recalling that $\langle \hat{\mu}^k, B_k \phi \rangle = 0$, then

$$\begin{aligned}
& \left| \sqrt{\epsilon(k)} \langle \mu_s^k, B_k \phi \rangle - \langle \xi_s^k, B \phi \rangle \right| = \\
& = \left| \langle \xi_s^k, B_k \phi - B \phi \rangle \right| \leq \\
& \leq \sqrt{\epsilon(k)} \left(k \sup_{i=0, \dots, k-1} |B_k \phi - B \phi| \left(\frac{i}{k} \right)^{\frac{1}{2}} \right. \\
& \quad \cdot \left. \sum_{i=0}^{k-1} |\mu_s^k(i/k) - \hat{\mu}^k(i/k)|^2 \right)^{\frac{1}{2}} \\
& \leq \text{const.} \sqrt{\frac{\epsilon(k)}{k}} \left(\sum_{i=0}^{k-1} |\mu_s^k(i/k) - \hat{\mu}^k(i/k)|^2 \right)^{\frac{1}{2}}
\end{aligned}$$

where the constant depends on $v(\cdot)$ and $\|\phi\|_3^E$.

Now the thesis follows by taking expectations and taking into account theorem 2.

§ 6. CENTRAL LIMIT THEOREM: CONVERGENCE

Till now we have characterized any limit point Q as a solution of the MPG

$$\begin{aligned}
F(\langle \xi_t, \phi \rangle) - \int_0^t F'(\langle \xi_s, \phi \rangle) \langle \xi_s, B\phi \rangle ds - \\
- \frac{1}{2} \sum_{ij} q_{ij} \phi(i) \phi(j) \int_0^t F''(\langle \xi_s, \phi \rangle) ds
\end{aligned}
\tag{6.1}$$

is a Q-martingale, for any $f(\cdot) = F(\langle \cdot, \phi \rangle) \in \mathcal{D}_A$ with $Q(\xi_0' = 0) = 1$.

Moreover, the processes $\langle \xi_t, \phi \rangle$ are Q-a.s. continuous (see Remark § 4).

Another equivalent characterization of such limit point is:

$$R_t^\phi := \langle \xi_t, \phi \rangle - \int_0^t \langle \xi_s, B\phi \rangle ds \tag{6.2}$$

$$S_t^\phi := \langle \xi_t, \phi \rangle^2 - 2 \int_0^t \langle \xi_s, \phi \rangle \langle \phi_s, B\phi \rangle ds - t \sum_{ij} q_{ij} \phi(i) \phi(j)$$

are continuous Q-martingales for any $\phi \in E$, $B\phi \in E$.

One can prove the direct implication noting that R_t^ϕ , S_t^ϕ are integrable with respect to any limit point Q

The remaining implication is based on Itô's formula and

$$\ll R^\phi \gg_t = t \sum_{ij} q_{ij} \phi(i) \phi(j) \tag{6.3}$$

with respect to any solution of the MGP (6.2).

The E' -valued process R_t such that $R_t^\phi = \langle R_t, \phi \rangle$ is uniquely determined by a duality argument as the solution of the MGP

$$F(\langle R_t, \phi \rangle) - \frac{1}{2} \sum_{ij} q_{ij} \phi(i) \phi(j) \int_0^t F''(\langle R_s, \phi \rangle) ds$$

is a martingale, and therefore it can be represented as

$$R_t := \sum_i w_i(t) \delta_i \tag{6.4}$$

where $(w_1(t), w_0(t), w_1(t))$ is a brownian motion with covariance matrix (q_{ij}) , and therefore the process ξ_t is uniquely determined in distribution as

$$\langle \xi_t, \phi \rangle := \sum_i \int_0^t (e^{(t-s)B} \phi)(i) dw_i(s) .$$

The uniqueness then proves the convergence.

We conclude by remarking that this kind of model fits sufficiently well in some applications.

Nevertheless, in the biological literature the problem arises allowing some kind of interaction in the population.

From the mathematical point of view this leads to the study of non linear Markov Processes, and in this direction we are now working.

REFERENCES

- (B.G.G.) Bertuzzi, A., Gandolfi, A., Giovenco, M.A.: "Mathematical Models of Cell Cycle with a View to Tumor Studies", Math. Biosci. 53, 159 (1981)
- (D.) Dawson, D.: "Stochastic measure diffusion processes", Canad. Math. Bull. 22, 129-138 (1979)
- (E.K.) Ethier, S.N., Kurtz, T.G.: "Markov Processes: characterization and convergence", J. Wiley & Sons (1986)
- (F.V.) Fleming, W.H., Viot, M.: "Some measure-valued Markov Processes in Populations Genetics Theory", Indiana University Math. J., 28 n. 5 (1979)
- (G.N.) Gerardi, A., Nappo, G.: "DNA Distribution as a Measure-valued Process", in "Stochastic Differential Systems", L.N. in Cont. and Inf. Sci. n. 69, Springer-Verlag (1985)

- (M.) Mitoma, I.: "Tightness of Probabilities on $C([0,1]; S')$ and $D([0,1]; S')$ ". Ann. Probab. 11, 4, 989-999 (1983)
- (R.) Rubinow, S.I.: "A Maturity-time Representation for all Populations", Biophys. J. 8 (1968) .

MAIN SHOP ☒		Job N ^o 89671	
Sub. Acct.	Fund	Dept. No.	Budget
	0624	5381	02
Department Inst. for Math and its Appl.			
Date of Order 4-14		Date Wanted 4-28	AM ☐ PM ☐
For further questions contact: Patricia			Phone: 4-6869
Call when ready for pickup: ☐			
Phone: Name:			
Deliver to: 545 V... Hall			

BINDERY ONLY ☐	OFFSET ☒
STOCK ONLY ☐	COMPOSITION ☐

Job Title: Martingale Approach....	
Ink/covers: Rembrandt Brown	
200 of 27 + covers	
(See pag.)	
Run Size $8\frac{1}{2}$ x 11 Trim Size _____ x _____ Finish Size $8\frac{1}{2}$ x 11 One Side ☐ Two Sides ☒	
PAPER PRINT CARRIERS	Body
	White 20# Sulphite $8\frac{1}{2}$ x 11
	White 60# OFFSET $8\frac{1}{2}$ x 11 ☒
	Other:
Cover	Kind Sundance Weight 65# Color Desert Bronze Size $8\frac{1}{2}$ x 11
Remarks:	
Elec. Masters ☒	
Megas! ☐	
Metal Plts. ☐	

BINDERY ☒	
COLLATE ☒	
BINDING:	GBC Binding ☐ Perfect ☐ Tape ☐ Shrink/Plastic Wrap ☐ Banding ☐
STITCHING:	Left Corner ☐ 2 on Side ☒ Saddle ☐
FOLDING:	For #10's ☐ $\frac{1}{2}$ Fold ☐ OTHER:
OTHER:	Drill ☐ 2-hole ☐ 3-hole ☐ Perforate ☐ Score ☐ Count in 100's ☐
Cutting ☐	Trimming ☐ Pad: NCR ☐ Glue ☐ Pads of _____ sheets/sets

Additional Instructions:

Patricia
K...
56

MARTINGALE APPROACH FOR MODELING DNA SYNTHESIS

BY

A. GERARDI

AND

G. NAPPO

IMA Preprint Series # 301

April 1987

INSTITUTE FOR MATHEMATICS AND ITS APPLICATIONS
UNIVERSITY OF MINNESOTA
514 Vincent Hall
206 Church Street S.E.
Minneapolis, Minnesota 55455

#	Author(s)	Title	Recent IMA Preprints (continued)	#	Author(s)	Title
165	D. Arnold and R.S. Falk,	Continuous Dependence on the Elastic Coefficients for a Class of Anisotropic Materials	203	G. Buttazzo, G. Dal Maso and U. Mosco,	A Derivation Theorem for Capacities with Respect to a Radon Measure	
166	J.J. Bakelman,	The Boundary Value Problems for Non-linear Elliptic Equation and the Maximum Principle for Euler-Lagrange Equations	204	S. Cowin, M. Mehrabadi,	On the Identification of Material Symmetry for Anisotropic Elastic Materials	
167	Ingo Müller,	Gases and Rubbers	205	R.W.R. Darling,	Constructing Nonhomeomorphic Stochastic Flows.	
168	Ingo Müller,	Pseudoelectricity In Shape Memory Alloys - an Extreme Case of Thermoelasticity	206	M. Chipot,	On the Reynolds Lubrication Equation	
169	Luis Magdalena,	Persistence and Smoothness of Hyperbolic Invariant Manifolds for Functional Differential Equations	207	R.V. Kohn and G.W. Milton,	On Bounding the Effective Conductivity of Anisotropic Composites	
170	A. Daniilman and M. Vogelius,	Homogenization Limits of the Equations of Elasticity in Thin Domains	208	I.J. Bakelman,	Notes Concerning the Torsion of Hardening Rods and Its N-Dimensional Generalizations	
171	H.C. Simpson and S.J. Spector,	On Hadamard Stability in Finite Elasticity	209	I.J. Bakelman,	The Boundary Value Problems for Non-linear Elliptic Equations	
172	J.L. Vazquez and C. Yarrur,	Isolated Singularities of the Solutions of the Schrödinger Equation with a Radial Potential	210	Guanglu Gong & Mingping Qian,	On the Large Deviation Functions of Markov Chains	
173	G. Dal Maso and U. Mosco,	Wiener's Criterion and T-Convergence	211	Arle Leizarowitz,	Control Problems with Random and Progressively Known Targets	
174	John H. Maddocks,	Stability and Folds	212	R.W.R. Darling,	Ergodicity of a Measure-Valued Markov Chain Induced by Random Transformations	
175	R. Hardt and D. Kinderlehrer,	Existence and Partial Regularity of Static Liquid Crystal Configurations	213	G. Gong, M. Qian & Zhongxin Zhao,	Killed Diffusions and Its Conditioning	
176	M. Nerukar,	Construction of Smooth Ergodic Cocycles for Systems with Fast Periodic Approximations	214	Arle Leizarowitz,	Controlling Diffusion Processes on Infinite Horizon with the Overtaking Criterion	
177	J.L. Erickson,	Stable Equilibrium Configurations of Elastic Crystals	215	Milard Beatty,	The Poisson Function of Finite Elasticity	
178	Patricio Aviles,	Local Behavior of Solutions of Some Elliptic Equations	216	David Terman,	Traveling Wave Solutions Arising From a Combustion Model	
179	S.-N. Chow and R. Lauterbach,	A Bifurcation Theorem for Critical Points of Variational Problems	217	Yuh-Jia Lee,	Sharp Inequalities and Regularity of Heat Semi-Group on Infinite Dimensional Spaces	
180	R. Pego,	Phase Transitions: Stability and Admissibility in One Dimensional Nonlinear Viscoelasticity	218	D. Stroock,	Lecture Notes	
181	Mariano Glaumata,	Quadratic Functions and Partial Regularity	219	Claudio Canuto,	Spectral Methods and Maximum Principle	
182	J. Bona,	Fully Discrete Galerkin Methods for the Korteweg De Vries Equation	220	Thomas O'Brien,	A Two Parameter Family of Pension Contribution Functions and Stochastic Optimization	
183	J. Maddocks and J. Keller,	Mechanics of Robes	221	Takeyuki Hida,	Analysis of Brownian Functionals	
184	F. Bernis,	Qualitative Properties for some nonlinear higher order Nonlinear Higher Order Parabolic Equations with Absorption	222	Leonid Hurwicz,	On Informational Decentralization and Efficiency of Resource Allocation Mechanisms	
185	F. Bernis,	Finite Speed of Propagation and Asymptotic Rates for some Nonlinear Higher Order Parabolic Equations with Minimal Strategy Spaces	223	E.B. Fabes and D.W. Stroock,	A New Proof of Moser's Parabolic Harnack Inequality via the Old Ideas of Nash	
186	S. Reichelstein and S. Reiter,	Game Forms with Minimal Strategy Spaces	224	Minoru Murata,	Structure of Positive Solution to $(-\Delta+V)u = 0$ in R^n	
187	J. Rubinstein and R. Mauri,	Dispersion and Convexity in Periodic Media	225	Paul Dupuis,	Large Deviations Analysis of Reflected Diffusion	
188	J. Rubinstein and P.E. Souganidis,	Asymptotic Series and the Method of Vanishing Viscosity	226	F. Bernis,	Existence Results for Doubly Nonlinear Higher Order Parabolic Equations on Unbounded Domains.	
189	W.H. Fleming and P.E. Souganidis,	Asymptotic Series and the Method of Vanishing Viscosity	227	S. Orey and S. Pelikan,	Large Deviations Principles for Stationary Processes of Minimal Surfaces.	
190	H. Beltrao Da Veiga,	Existence and Asymptotic Behavior for Strong Solutions of Navier-Stokes Equations in the Whole Space	228	R. Gulliver and S. Hildebrandt,	Boundary Configurations Spanning Continua	
191	L.A. Caffarelli, J.L. Vazquez, and N.I. Wolanski,	Lipschitz Continuity of Solutions and Interfaces of the N-Dimensional Porous Medium Equation	229	J. Baxter, G. Dal Maso and U. Mosco,	Stopping Times and T-Convergence.	
192	R. Johnson,	m-Functions and Floquet Exponents for Linear Differential Systems	230	Juilio Bouilliet,	Self-Similar Solutions, Having Jumps and Intervals of Constancy of a Diffusion-heat Conduction Equation	
193	F.V. Atkinson and L.A. Peletier,	Ground States and Dirichlet Problems for $-\Delta = F(U)$ in R^n	231	R. Hardt, D. Kinderlehrer & F.-H. Lin,	A Remark About the Stability of Smooth Equilibrium Configurations of Static Liquid Crystal	
194	G. Dal Maso, U. Mosco,	The Wiener Modulus of a Radial Measure	232	M. Chipot and M. Luskin,	The Compressible Reynolds Lubrication Equation	
195	H. A. Levine and H.F. Weinberger,	Inequalities between Dirichlet and Neumann Eigenvalues	233	J.H. Maddocks,	A Model for Disclinations in Nematic Liquid Crystal	
196	J. Rubinstein,	On the Macroscopic Description of Slow Viscous Flow Past a Dirichlet Problem	234	C. Fofas, G.R. Sell and R. Temam,	Inertial Manifolds for Nonlinear Evolutionary Equations	
197	G. Dal Maso and U. Mosco,	Wiener Criteria and Energy Decay for Relaxed Dirichlet Problems	235	P.L. Chow,	Expectation functionals Associated with Some Stochastic Evolution	
198	V. Ojker and P. Walfman,	On the Monge-Ampere Equation Arising in the Reflect Mapping Problem	236	Giuseppe Buttazzo,	Reinforcement by a Thin Layer with Oscillating Thickness	
199	M. Chipot, D. Kinderlehrer and L. Caffarelli,	Some Smoothness Properties of Linear Laminaes	237	W.H. Fleming, S.J. Sheu and H.M. Soner,	On Existence of the Dominant Eigenfunction and Its Application to the Large Deviation Properties of a Ergodic Markov Process	
200	Y. Giga and R. Kohn,	Characterizing Blow-up Using Similarity Variables	238	R. Jensen and P.E. Souganidis,	A Regularity Result for Viscosity Solutions of Hamilton-Jacobi Equations in one Space Dimension	
201	P. Cannarsa and H. M. Soner,	On the Singularities of the Viscosity Solutions to Hamilton-Jacobi-Bellman Equations	239	B. Boczar-Karakl, J.L. Bona and D.L. Cohen,	Interaction of Shallow-Water Waves and Bottom Topography	
202	Andrew Majda,	Nonlinear Geometric Optics for Hyperbolic Systems of Conservation Laws	240	F. Colomius and W. Kliemann,	Infinite Time Optimal Control and Periodicity	

Author(s)	Title	Recent IMA Preprints (continued)	Author(s)	Title
2241 Harry Keesten,	Scaling Relations for 2D-Percolation	227 Cockburn, B.	The Quasi-Monotone Schemes for Scalar Conservation Laws Part II	
2242 A. Leizorowitz,	Infinite Horizon Optimization for Markov Process with Finite States Spaces	278 M. Chipot, T. Sideris,	On the Abelian Higgs Model	
2243 Louis H.-Y. Chen,	The Rate of Convergence in A Central Limit Theorem for Dependent Random Variables with Arbitrary Index Set	279 C. Fofas, B. Nicolaeenko, G.R.Sell, R. Temam,	Inertial Manifolds for the Kuramoto-Sivashinsky Equation and an Estimate of their Lowest Dimension	
2244 G. Kallianper,	Stochastic Differential Equations in Duals of Nuclear Spaces with some Applications	280 R. Duran,	On the Approximation of Miscible Displacement in Porous Media by a Method of Characteristics Combined with a Mixed Method	
2245 Tzuu-Shuh Chiang,	Yunshong Chow and Yuh-Jia Lee, Evaluation of Certain Functional Integrals	281 H. Axiang, Zhang Bo,	The Convergence for Nodal Expansion Method	
2246 L. Karp and M. Pinsky,	The First Eigenvalue of a Small Geodesic Ball in a Riemannian Manifold	282 V. Tverksy,	Dispersive Bulk Parameters for Coherent Propagation in Correlated Random Distributions	
2247 Chi-Sing Lam,	Towards An Acoustoelastic Theory for Measurement of Residual Stress	283 W.Th.F. den Hollander,	Mixing Properties for Random Walk in Random Scenery	
2248 Andreas Stoll,	Invariance Principles for Brownian Intersection	284 H.R. Jauslin,	Nondifferentiable Potentials for Nonequilibrium Steady States	
2249 R.W.R. Darling,	Local Time and Polymer Measures	285 K. Meyer, G.R.Sell,	Homoclinic Orbits and Bernoulli Bundles in Almost Periodic Systems	
2250 R. Cohen, R. Hardt, D. Kinderlehrer, S.Y.Lin, M. Luskin,	Minimum Energy for Liquid Crystals: Computational Results	286 J. Douglas, Jr., Y. Yuan,	Finite Difference Methods for the Transient Behavior of a Semiconductor Device	
2251 Suzanne M. Lehnert,	Viscosity Solutions for Weakly Coupled Systems of First Order PDEs	287 Li Kaitai, Yan Mingming,	The Extrapolation for Boundary Finite Elements	
2252 M. Cranston, E. Fales, Z. Zhao,	Condition Gauge and Potential Theory for the Schrödinger Operator	288 R. Durrett, R.H. Schonman,	Stochastic Growth Models	
2253 H. Brezis, J.M.Coron, E.M. Lieb,	Harmonic Maps with Defects	289 David Kinderlehrer,	Remarks about Equilibrium Configurations of Crystals	
2254 A. Carverhill,	Flows of Stochastic Dynamical Systems: Nontriviality of the Lyapunov Spectrum	290 D.G. Aronson, J.L. Vazquez,	Eventual C^∞ -Regularity and Concavity for Flows in One-Dimensional Porous Media	
2255 A. Carverhill,	Conditioning A 'Lifted' Stochastic System in a Product Case	291 L.R. Scott, J.M. Boyle, B. Bagheri,	Distributed Data Structures for Scientific Computation	
2256 R.J. Williams,	Local Time and Excursions of Reflected Brownian Motion	292 J. Douglas, Jr., P.J.Paes Leme, T. Arbogast, T. Schmitt,	Simulation of Flow in Naturally Fractured Petroleum Reservoirs	
2257 H. Föllmer, S. Grey,	Large Deviations for the Empirical Field of a Gibbs Measure	293 D.G. Aronson, L.A. Caffarelli,	Optimal Regularity for One-Dimensional Porous Medium Flow	
2258 A. Leizorowitz,	Characterization of Optimal Trajectories On an Infinite Horizon	294 Helin Brezis,	Liquid Crystals and Energy Estimates for S^2 -Valued Maps	
2259 Y.Giga, T. Miyakawa, H. Osada,	Two Dimensional Navier Stokes Flow with Measures As Initial Vorticity	295 Todd Arbogast,	Analysis of the Simulation of Single Phase Flow Through a Naturally Fractured Reservoir	
2260 M. Chipot, V. Ollier,	Sur une Propriete Des Fonctions Propres De L'operateur De Laplace Beltrami	296 He Yiminian, Li Kaitai,	The Coupling Method of Finite Elements and Boundary Elements for Radiation Problems	
2261 V. Perez-Abreu,	Decompositions of Semimartingales On Duals of Countably Nuclear Spaces	297 T. Cazenave, A. Haraux, L. Vazquez, F.B. Weissler,	Nonlinear Effects in the Wave Equation with a Cubic Restoring Force	
2262 J.M. Ball,	Does Rank-One Convexity Imply Quasiconvexity	298 M. Chipot, F.B. Weissler,	Some Blow Up Results for a Nonlinear Parabolic Parabolic Equation with a Gradient Term	
2263 B. Cockburn,	The Quasi-Monotone Schemes for Scalar Conservation Laws. Part I	299 Li Kaitai,	Perturbation Solutions of Simple and Double Bifurcation Problems	
2264 K.A. Pericak-Spector,	On Radially Symmetric Simple Waves in Elasticity	300 Chen Zhanxin, Li Kaitai,	The Convergence on the Multigrid Algorithm for Navier-Stokes Equations	
2265 P.M. Shivakumar, Chi-Sing Man, Simon W. Rabkin,	Modelling of the Heart and Pericardium at End-Diastole	301 A. Gerardi, G. Nappo,	Martingale Approach for Modeling DNA Synthesis	
2266 Jose-Luis Menaldi,	Probabilistic View of Estimates for Finite Difference Methods	302 D.N. Arnold, L. Ridgway Scott Michael Vogelius,	Regular Inversion of the Divergence Operator with Dirichlet Boundary Conditions on a Polygon	
2267 Robert Hardt,	Harold Rosenberg, Open Book Structures and Unicity of Minimal Submanifolds	303 Duran, Ricardo G.	Error Analysis in L^p , $1 \leq p \leq \infty$, for Mixed Definite Elements	
2268 Bernardo Cockburn,	The Quasi-Monotone Schemes for Scalar Conservation Laws	304 Nochetto, Ricardo H., Verdi, Claudio,	An Efficient Linear Scheme to Approximate Parabolic Free Boundary Problems: Error Estimates and Implementation	
2269 H.R. Jauslin, W. Zimmermann, Jr.,	Dynamics of a Model for an Ac Josephson Effect in Superfluid 4He	305 K.A. Pericak-Spector, Scott J. Spector,	Nonuniqueness for a Hyperbolic System	
2270 A.K. Kapila,	Introductory Lecture on Reacting Flows	306 E.G. Kalnins, Willard Miller, Jr.,	q-Series and Orthogonal Polynomials Associated with Bernes' First Lemma	
2271 J.C. Taylor,	Do Minimal Solutions of Heat Equations Characterize Diffusions?	307 D.N. Arnold, Richard S. Falk,	A Uniformly Accurate Finite Element Method for Mindlin-Reissner Plate	
2272 J.C. Taylor,	The Minimal Eigenfunctions Characterize the Ornstein-Uhlenbeck Process	308 Chi-Wang Shu,	TVD Properties of a Class of ModifiedENO Schemes for Scalar Conservation Laws	
2273 Chi-Sing Man, Quan-Xin Sun,	On the Significance of Normal Stress Effects in the Flow of Glaciers	309 Edmund Dikow, Ulrich Horning,	A Random Boundary Value Problem Modeling Spatial Variability in Porous Media Flow	
2274 Omar Hijab,	On Partially Observed Control of Markov Processes	310 Jack K. Hale,	Compact Attractors and Singular Perturbations	
2275 Lawrence Gray,	The Behavior of Processes with Statistical Mechanical Properties	311 Bourgaet, A. Cockburn, B.,	The TVD-Projection Method for Solving Implicit Numerical Schemes for Scalar Conservation Laws: A Numerical Study of a Simple Case	
2276 R. Hardt, D. Kinderlehrer, M. Luskin,	Remarks About the Mathematical Theory of Liquid Crystals			