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Introduction

This conference is part of the SPIE's 2001 Symposium on Microelectronics and MEMS, held at the Stamford Plaza Hotel, Adelaide, Australia. Three other parallel conferences are being held as part of this symposium: (i) Electronics and Structures for MEMS, (ii) Device and Process Technologies for MEMS and Microelectronics, and (iii) Design, Characterization, and Packaging for MEMS and Microelectronics.

The papers in these proceedings represent some of the latest research issues in the design and technology of bioMEMS and smart nanostructures. BioMEMS, biomimetics, nanomaterials, and microfluidics are all represented. It is pleasing to see a range of papers on nanotechnology issues for quantum computation. In order to promote stimulating discussion, we included a Round Table discussion on quantum computation called "Can practical tasks be performed by quantum computers?" The issue of noise and fluctuation, a key aspect in nanotechnology and bioinformatics, is addressed by several authors.

In order to comply with the requirements of some institutions, the authors were able to have their manuscripts reviewed by the international technical committee. Review was judged on the basis of originality, substance, technical quality, and significance.

Authors were invited to submit extended papers to the IOP's journal of *Smart Materials and Structures* to be published in a special issue that will appear later in 2002.

A big thanks is due to the symposium chairs, Derek Abbott (Adelaide University, Australia) and Vijay K. Varadan (The Pennsylvania State University, USA), for their splendid work. A special thanks goes to my cochairs Erol Harvey and Bill Spillman, and to the Program Committee for their support and labor.

Finally, our appreciation must go to the authors for sharing their work, the attendees for their stimulating questions, and both the authors and attendees for their enthusiasm. The resulting interaction will make this a most productive and enjoyable conference.

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How much power does neural signal propagation need?

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ABSTRACT

Two well known, biologically inspired non-dynamical models of stochastic resonance, the threshold-crossing model and the fluctuating rate model are analyzed in terms of channel information capacity and dissipation of energy necessary for small-signal transduction. Using analogies to spike propagation in neurons we postulate the average output pulse rate as a measure of dissipation. The dissipation increases monotonically with the input noise. We find that for small dissipation both models give an asymptotically linear dependence of the channel information capacity on dissipation. In both models the channel information capacity, as a function of dissipation, has a maximum at input noise amplitude that is different from that in the standard signal-to-noise ration vs. input noise plot. Though a direct comparison is not straightforward, for small signals the threshold model gives appreciably higher density of information per dissipation than the exponential fluctuating rate model. We show that a formal introduction of cooperativity in the rate fluctuating model permits us to imitate the response function of the threshold model and to enhance performance. This finding may have direct relevance to real neural spike generation where, due to a strong positive feedback, the ion channel currents are adding up in a synchronized way.

Keywords: Neuron, ion channel, energy dissipation, information transfer

1. INTRODUCTION

Noise-facilitated signal transduction, or stochastic resonance,[1] SR, is attracting significant attention (for reviews see[6,18,19]). Here we consider two well-known non-dynamical models of noise-facilitated signal transduction from the point of view of energy dissipation. The first model, introduced six years ago,[7,10] is a threshold model where a pulse (or a spike) is generated every time the input parameter comprised of signal and noise reaches the threshold voltage value.[12] The second model, described four years ago,[2-4] is a threshold-free model of signal transduction. It is based on the so-called inhomogeneous Poisson process. In this process the rate of pulse generation is modulated by the input parameter in a continuous manner. By bypassing a discussion of the mechanistic origins of such processes, this model shows that a number of non-linear dependencies between the input stimulus and the process rate lead to SR demonstrating its universal character;[2] see also in another article.[5]

Pulse generation in both electronics and biology is a non-equilibrium process that dissipates energy. For example, a rough estimate that uses typical times (~1 ms), current densities (~1 mA/cm2), and voltages (~0.1V) for a squid giant axon shows that,[9] to produce a spike, the axon dissipates about 10^{-7} J/cm^2. The free energy of adenosine triphosphate (ATP) hydrolysis is close to 3.104 J/mol,[17] therefore propagation of an action potential over a square centimeter of axon surface requires hydrolysis of about 2.1012 ATP molecules. This is the cost of an elementary step in biological information processing. Guided by this consideration, we will compare the two SR models taking the rate of output pulse generation as a measure of dissipation.

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2. COMPARISON OF THE MODELS

In the present paper, we restrict our considerations to the case of small and adiabatically slow signals. We start with Shannon's formula for the channel information capacity I to show that, for small signals, this measure coincides with the signal-to-noise ratio (SNR). The channel information capacity characterizes the rate of information transmission (dimensions: bits/second) and, for a white spectral distribution of the output noise, can be written in the form:[13]

$$I = B_{out}\log_a\left(1+\frac{P_s}{S_{n\,out}B_{out}}\right), \tag{1}$$

where B_{out} is the output frequency bandwidth, P_s is the output signal power, and $S_{n\,out}$ is the spectral density of the output noise. It is clear that for small harmonic signals with $S_s(f)=\left(A^2/2\right)\delta(f-f_s)$, where A is signal amplitude and f_s is signal frequency, the integration of Eq.(1) gives:

$$I \cong \frac{1}{\ln a}\frac{A^2/2}{S_{n\,out}}. \tag{2}$$

It is interesting that due to the low signal limit, which has a key importance in practical biological applications, this expression differs from the standard definition of the SNR frequently used in noise-facilitated signal transduction studies only by a factor $1/\ln a$ which accounts for the choice of the base of the information measure.
In the small-signal adiabatic approximation the analytical expression describing channel information capacity in the threshold-crossing model is obtained from its output SNR as:[11]

$$I_{fr} = \frac{SNR_{th}}{\ln 2} = \frac{2}{\sqrt{3}\ln 2}B_n\frac{\left(AU_t\right)^2}{\left(B_nS_n\right)^2}\exp\left(\frac{-U_t^2}{2B_nS_n}\right), \tag{3}$$

where the corresponding mean firing rate characterizing the dissipation is as follows:

$$D_{th} = \left\langle r_{th}(t)\right\rangle = \frac{B_n}{\sqrt{3}}\exp\left(\frac{-U_t^2}{2B_nS_n}\right). \tag{4}$$

Here B_n and S_n are frequency bandwidth and spectral density of the input noise and U_t is the threshold height. A rectangular spectral shape of the input noise is assumed here. For the input noise represented by an Ornstein-Uhlenbeck process the numerical multiplicative factor is different[10].

For the fluctuating rate model,[3,4] where the pulse generation rate $r(t)$ is the following function of the input parameter $V(t)$:

$$r_{fr}(t) = r(0)\exp\left(\beta V(t)\right), \tag{5}$$

the dissipation is

$$D_{fr} = \left\langle r_{fr}(t)\right\rangle = r(0)\exp\left(\frac{\beta^2 B_nS_n}{2}\right). \tag{6}$$

In the same approximation as above the channel information capacity is given by:

$$I_{fr} = \frac{SNR_{fr}}{\ln 2} = \frac{(\beta A)^2}{2\ln 2} \frac{\nu(0)\exp\left(\frac{\beta^2 B_n S_n}{2}\right)}{2 + \frac{\nu(0)}{B_n}\exp\left(\frac{\beta^2 B_n S_n}{2}\right)\sum_1^{\infty}\frac{\left(\beta^2 B_n S_n\right)^m}{m!\,m}}. \quad (7)$$

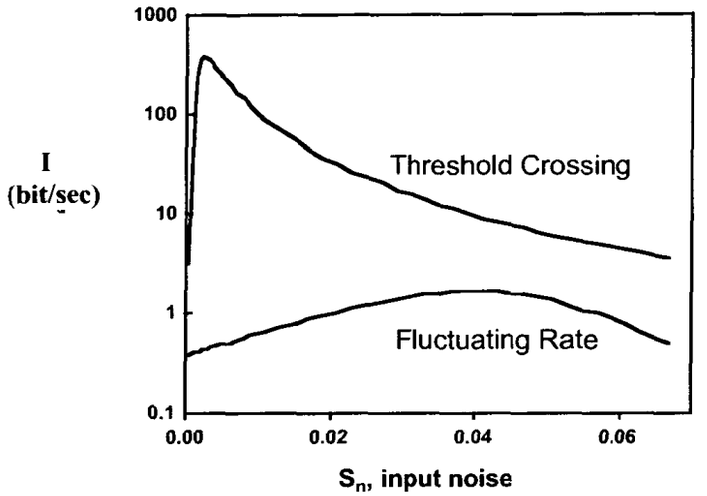

Fig. 1. Maxima in the information capacity in the two models differ by two orders of magnitude with about ten-fold different optimal spectral densities of the input noise.

We can compare two models using the following parameters: $U_t = 1$, $\beta = 1$, $\nu(0) = 1$, $B_n = 100$. Figure 1 shows the channel information capacity as a function of the input noise spectral density demonstrating two features. First, the threshold-crossing model gives an information capacity maximum at about ten times smaller input noise intensity than the fluctuating rate model. Second, the information capacity at the threshold-crossing model maximum is significantly higher. This qualitative behavior is observed at every combination of $\nu(0)$ and B_n, as long as condition $\nu(0) < B_n$, necessary for the stochastic resonance onset in the fluctuating-rate model, is fulfilled.[2,4]

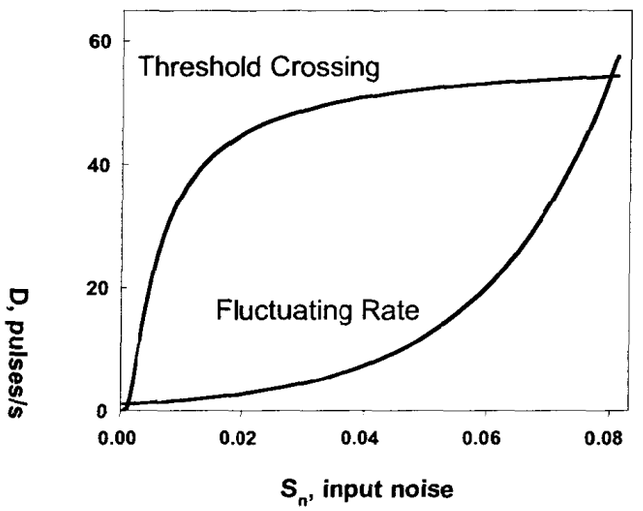

Fig. 2. Dissipation as a function of the input noise spectral density shows quite different qualitative behavior.

The dissipation, as a function of the input noise spectral density, is presented in Figure 2. It is obvious that the qualitative behavior in the two models is quite different. The threshold-crossing model demonstrates saturation to a level, which is expected in the case of strong input noise, where the number of crossings is defined by the noise spectral

composition[12]. The fluctuating-rate model shows exponential growth of dissipation.

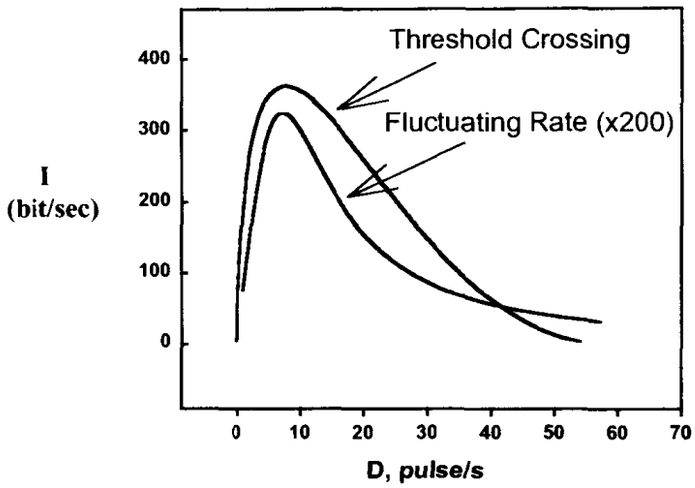

Fig. 3. Information capacity as a function of dissipation is qualitatively similar.

Figure 3 displays the information capacity as a function of dissipation. It can be seen that, in the two models, the maxima in information capacity occur at close values of dissipation. However, the ratio of information capacity to dissipation is about two orders of magnitude higher in the threshold-crossing model.

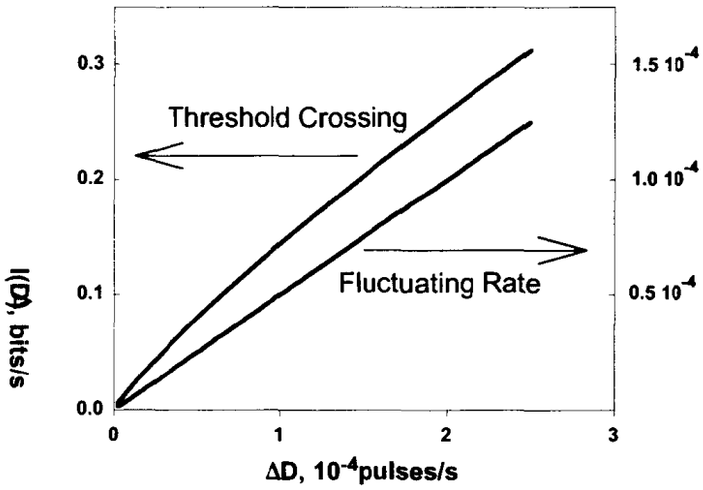

Fig. 4. In both models gain in the information capacity in the limit of low dissipation is approximately proportional to dissipation.

Figure 4 illustrates the information capacity vs. dissipation at small dissipations. It is seen that in the fluctuating rate model the relationship is linear and in the threshold-crossing model it is close to linear. Using Eqs. 3-7, it is easy to show that at small dissipations

$$I_{th} \cong \frac{8}{\ln 2}\left(\frac{A}{U_t}\right)^2 \left(\ln D_{th}\right)^2 D_{th} \tag{8}$$

and

$$\Delta I_{fr} \cong \frac{\left(\beta A\right)^2}{2\ln 2}\Delta D_{fr} \tag{9}$$

where ΔI_{fr} and ΔD_{fr} are the noise-induced increments in information capacity and dissipation (in the case of the threshold-crossing model $\Delta I_{th} = I_{th}$ and $\Delta D_{th} = D_{th}$). The comparison of Figs. 1-3 and Eqs. 8 and 9 shows that the threshold-crossing model serves as a much more efficient signal transducer in terms of information-to-dissipation ratio. Indeed, the threshold characteristic can be seen as a limiting case of exponential dependence where parameter β is large. For the rest of the parameters as specified above and at dissipations close to optimal (Fig.2), the fluctuating rate model

gives information-to-dissipation ratios similar to those in the threshold-crossing model at $\beta \approx 7$.

The encoding of information into nerve pulse trains is a vividly discussed unsolved problem.[15,16] The results discussed above relate to the pulse rate modulation mechanism, believed to be dominating in many studied examples.[14] By comparing the information content of the transduced signals with the corresponding dissipation we show that the two models, both using basically the same pulse rate modulation mode of signal encoding, are significantly different in their efficiency.

As an immediate biological application - nerve pulse generation - is concerned, the following paradox is now apparent. Ion channel dynamics can be approached by the fluctuating rate model[4,8] and neuron firing dynamic by the threshold model[12]. On the other hand, neuron firing events, which are dissipation optimized, are collective phenomena of ion channel opening events, which have poor dissipation performance. It is clear that the dissipation, produced by ion channel transient opening/closing events, adds up to give the overall dissipation during neuron firing. Therefore, the nontrivial question is how a system can be optimized for dissipation while its elements seem to be not. The possible solution of this paradox is that during pulse generation ion channels act cooperatively because of a strong positive feedback via the membrane potential of the excitable nerve cell.

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DNA computing in microreactors

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ABSTRACT

The goal of this research is to improve the modular stability and programmability of DNA-based computers and in a second step towards optical programmable DNA computing. The main focus here is on hydrodynamic stability. Clockable microreactors can be connected in various ways to solve combinatorial optimisation problems, such as Maximum Clique or 3-SAT. This work demonstrates by construction how one micro-reactor design can be programmed to solve any instance of Maximum Clique up to its given maximum size (N). It reports on an implementation of the architecture proposed previously [1]. This contrasts with conventional DNA computing where the individual sequence of biochemical operations depends on the specific problem. In this pilot study we are tackling a graph for the Maximum Clique problem with N≤12, with a special emphasis for N=6. Furthermore, the design of the DNA solution space will be presented, which is symbolised by a set of bit-strings (words).
Keywords: DNA, microflow reactor, programmability, maximum clique.

INTRODUCTION

DNA computing involves a multidisciplinary interplay between molecular biology, information science, microsystem technology, physical detection methods and evolution. Since the first practical example of DNA computing by Adleman [2] in 1994, there has been intensive research into the use of DNA molecules as a tool for calculations, simulating the digital information processing procedures in conventional computers. In the short term, however, the main application of DNA computing technology will be rather to perform complex molecular constructions, diagnostics and evolutionary tasks. In order to assess the limits of this technology, we are investigating a benchmark computational problem: Maximum Clique, chosen as an NP-complete problem because of its limited input information [3]. The step from batch processing in test tubes to pipelined processing in integrated micro-flow reactor networks, gives us complete control over the process of information flow and allows operations much faster than in conventional systems. More importantly, it allows programming.

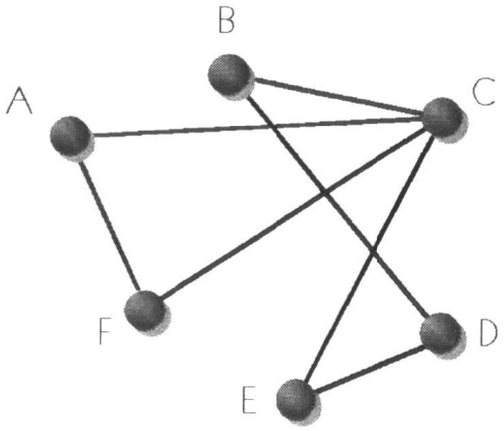

Figure 1. *An N=6 instance of the clique problem. The maximum clique is given by ACF, represented by 101001. BCDE is not a clique because C and D nor B and E are connected with each other.*

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BENCHMARK PROBLEM

MAXIMUM CLIQUE

The decision problem associated with the maximum clique problem becomes rapidly harder to solve (it is NP-complete) as the problem size increases. Maximum clique requires finding the largest subset of fully interconnected nodes in the given graph (*e.g.*, Fig. 1). To obtain the set of cliques and then determine its largest member using a micro-flow system, an algorithm was devised consisting of a series of selection steps, each containing three parallel selection decisions [1].

The problem can be divided into two parts: (i) find all the subsets of nodes which correspond to cliques in the graph and (ii) find the largest one. The basic algorithm is simple: for each node i ($i \geq 1$) in the graph retain only subsets either not containing node i or having additionally only nodes j such that the edges (i,j) are in the graph. This can be implemented in two nested loops (over i and j), each step involving two selectors in parallel.

A third selector was introduced to allow the selector sequences to be fixed independently of the graph instance. Thus the graph dependence is programmed not by which but by whether a sub-sequence selection in the third selector is performed (see Fig. 2). It is important to note that only positive selection for sequences with the desired property is performed, not subtractive selection.

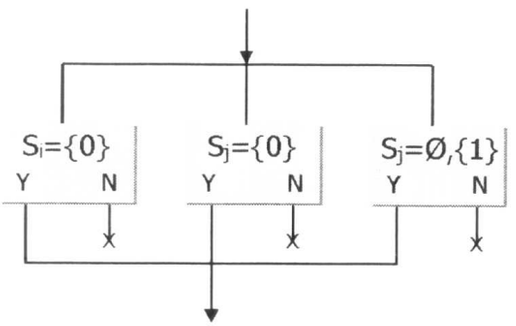

Figure 2. *A flow diagram showing the selection step for node subsets regarding 'cliqueness' at (i,j). The three modules reflect that either node i or nod j is absent or the edge (i,j) must be present in the graph.*

The edges of the graph, *i.e.* the connections between the nodes, can be represented by a so called connectivity matrix. The connectivity matrix for the 6-node example shown in Fig. 1 is the 6x6 matrix in Table 1. As Table 1 shows, the matrix is symmetrical over the diagonal, while the diagonal is trivially one, reducing the number of necessary selections from N^2 to ½N(N-1).

Table 1. *The connectivity matrix for the 6-node graph as shown in Fig. 1. The shaded numbers are trivial selections and don't have to be included in the selection procedure to obtain all the cliques.*

	A	B	C	D	E	F
A	1	0	1	0	0	1
B	0	1	1	1	0	0
C	1	1	1	0	1	1
D	0	1	0	1	1	0
E	0	0	1	1	1	0
F	1	0	1	0	0	1

SELECTION PROCEDURE

Each DNA sequence encodes a binary sequence corresponding to a particular subset of nodes in the graph. Different DNA sub-sequences are used to represent presence (1) or absence (0) at each node. As shown in Fig. 2, each selection step consists of 3 selectors in parallel. After each selection step, the sub-population is passed on to the next selection