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White noise analysis of non-linear systems
and its applications in biology

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Nonlinear system identification is one of the most interesting subjects which one meets in a variety of fields such as engineering, physics, and biology, although it may appear in a peculiar manner to each field. Numerous literature have been published on the theory and the practice, for which one may consult[1]. White noise analysis, often referred to as Wiener analysis after the pioneering work of Wiener[2], is known as powerful methodology to approach the identification problem. The method, as we shall explain in the subsequent sections, is based on full use of the familiar (but mathematically tricky) property of the Gaussian white noise, a formal derivative of the Brownian motion. For a given (time invariant and stable dynamical) system, its impulse response function (referred to as the first order kernel) and the higher order kernels(as the extensions of the impulse response function of a linear system to a nonlinear one) are sometimes called as Wiener kernels and characterize the system's output to the white noise input. There have been a number of works on Wiener analysis[3],[4],[5]. Some of them are on the relationship between the series and the traditional or conventional description of a system (for example [6],[7]). There are works on the applicability and the limitation of the

methods[8],[9]. There are also works concerning the problems which may arise in the practical use of the methods: How to measure the kernels[2],[10],[11], how to interpret the kernels measured[12] and so on.

In the past decade, Wiener analysis has seen a number of practical applications in biological system's analysis. In the application, the method is recognized to have several well-advertized advantages which are summerized as follows: (1) The method does not require a priori knowledge on the system to be analyzed. It can be thus classified into a non-parametric method of identification. Most of biological systems are 'blackboxes' and it is not always possible to 'peep' into the inside of the boxes. Even if one succeeds in doing so, there always are smaller blackboxes to be dealt with. In most of biological systems, we do not have any idea on the type of nonlinearity involved. It is not always possible, therefore, to identify a particular nonlinearity in a system and to describe it through individual or tailored theory. Under the circumstance a generalized (nonlinear) system analysis such as non-parametric methods seems to offer a better chance of identifying biological systems. (2) In principle, it suffices to acquire a rather shoter sequence of the simultaneous observations of the test input and the corresponding output in order to estimate the whole kernels. This is a crucial factor in biological applications[3].

In what follows, we will review the three aspects of the Wiener's method of nonlinear system analysis: (1) Mathematical background of the theory (2) Structure of time invariant systems and their Wiener kernels (3) Biological applications.

II. Mathematical background

The theory has been developed essentially as a mathematical means to represent a strictly stationary noise in terms of the Brownian motion [13], although Wiener, who originated the theory, foresaw the possibility of the theory's application in the statistical mechanics. In electrical and control engineering the theory is called 'white-noise analysis' and is used to analyze stable physical systems; a proper application in the case of linear systems. In his famous book, Wiener himself discussed the possibility of applying his theory to the practical, engineering problem [12].

Consider the Brownian motion $B(t)$, $-\infty < t < \infty$ defined on a probability space (Ω, \mathcal{F}, P) , where symbols are understood as usual. Let $L^2(B)$ be the totality of Brownian functionals ψ satisfying

$$E\psi(B)^2 < \infty \quad (1)$$

$L^2(B)$ can be a Hilbert space if the inner product and the norm are suitably defined. Therefore, the space $L^2(B)$ possesses an orthogonal base. One may adopt as the base the orthogonal system of multiple Wiener integrals. The multiple Wiener integral of order n can be viewed as a subspace of $L^2(B)$ [14], namely the image of $L^2(\mathbb{R}^n)$ (= totality of square summable functions defined on \mathbb{R}^n) by a linear map I_n defined as follows [15]: Let $k_n(t_1, \dots, t_n)$ be any element of $L^2(\mathbb{R}^n)$. Then

$$I_n(k_n; B(\cdot)) = \int_{-\infty}^{\infty} \int k_n(t_1, \dots, t_n) h^{(n)}(dB(t_1), \dots, dB(t_n)) \quad (2)$$

where k_n is referred to as the Wiener kernel of order n .

$h^{(n)}(dB(t_1), \dots, dB(t_n))$ is a function defined via multi-variate Hermite polynomials: Let $\{X_i\}_{i=1, \dots, N}$ be the independent random variables defined on (Ω, \mathcal{B}, P) , each subject to the Gaussian distribution with mean 0 and variance P_i . Then the function is defined as follows:

$$h^{(n)}(x_{i_1}, \dots, x_{i_n}) = \mathcal{H}_n\left(\frac{x_{i_1}}{P_{i_1}}, \dots, \frac{x_{i_n}}{P_{i_n}}\right) (P_{i_1} \dots P_{i_n})^{1/2} \quad (3)$$

where \mathcal{H}_n is the multivariate Hermite polynomial with respect to N variables x_1, \dots, x_N ;

$$\mathcal{H}_n(x_{i_1}, \dots, x_{i_n}) = (-1)^n \exp\left(\frac{1}{2} \sum_{i=1}^N x_i^2\right) \frac{\partial^n}{\partial x_{i_1} \dots \partial x_{i_n}} \exp\left(-\frac{1}{2} \sum_{i=1}^N x_i^2\right) \quad (4)$$

Therefore, any Brownian functional $\psi(B)$ can be expanded in the series of orthogonal functionals for a suitable choice of $\{k_n\}$:

$$\psi(B) = \sum_{n=0}^N I_n(k_n; B(\cdot)) \quad (5)$$

This implies that ψ can be characterized by the sequence of $\{k_n\}$. Now let us consider the output of a time invariant and "stable" physical system exposed to the Gaussian white noise input with mean 0 and variance 1. Since the noise is mathematically interpreted as a formal derivative of the Brownian motion $B(t)$, the system's output can be also regarded as the Brownian functional. The output of the stable system belongs to $L^2(B)$ and is expanded in a possibly infinite series of orthogonal functional of the Brownian motion. The system's output to any Gaussian white noise input can be determined by the series of orthogonal functionals which are specified by the kernels $\{k_n\}$. Note

that we may regard $k_n = k_n(t_1, \dots, t_n)$ as a symmetric function of the indicated arguments without loss of generality from the property of I_n [16]. For a given system ψ , the corresponding kernels can be computed as follows [16], [17]. Note that any $k_n(t_1, \dots, t_n) \in L^2(\mathbb{R}^n)$ is considered to be a limit of a sequence of step functions $\phi_n^{(N)}(t_1, \dots, t_n)$, $N=1, 2, \dots$, each defined on a product space of the same finite interval, $T^{(N)}$, i.e., on $T^{(N)} \times \dots \times T^{(N)} \subset \mathbb{R}^n$:

$$\phi_n^{(N)}(t_1, \dots, t_n) = \begin{cases} \phi_{i_1 \dots i_n} & \text{if } (t_1, \dots, t_n) \in \Delta_{i_1} \times \dots \times \Delta_{i_n} \\ 0 & \text{otherwise} \end{cases} \quad (6)$$

where $\Delta_i = [\tau_i, \tau_{i+1})$, $i=1, 2, \dots, N$ are non-overlapping intervals and are a partition of the finite interval $T^{(N)}$, and where each $|\Delta_i|$ ($|\Delta|$; Lebesgue measure of Δ) tends to 0 and $T^{(N)}$ to infinity as N goes to infinity. We denote by Δ the length of interval $|\Delta|$ as well as the interval itself. Now noting the symmetric property of k_n and hence $\phi_n^{(N)}$, $\phi_{i_1 \dots i_n}^{(N)}$ can be obtained as follows:

$$\phi_{i_1 \dots i_n}^{(N)} = \frac{1}{n! \Delta_{i_1} \dots \Delta_{i_n}} E \psi(B(\Delta_1), \dots, B(\Delta_N)) h^{(n)}(B(\Delta_{i_1}), \dots, B(\Delta_{i_n})) \quad (7)$$

$$(1 \leq i_1, \dots, i_n \leq N)$$

where we have replaced the Brownian functional $\psi(B)$ by a function of $B(\Delta_1), \dots, B(\Delta_N)$ and have rewritten the function as $\psi(B(\Delta_1), \dots, B(\Delta_N))$. As far as the output of time invariant and stable physical system concerns, it can be written as

$$\psi(\tau; \omega) = \sum_{n=0}^{\infty} I_n(k_n; B(\cdot + \tau; \omega))$$

$$\begin{aligned}
&= \sum_{n=0}^{\infty} \int_{-\infty}^{\infty} \dots \int_{-\infty}^{\infty} k_n(t_1, \dots, t_n) h^n(dB(\tau+t_1), \dots, \tau+t_n)) \\
&= \sum_{n=0}^{\infty} \int_{-\infty}^{\infty} \dots \int_{-\infty}^{\infty} k_n(t_1-\tau, \dots, t_n-\tau) h^{(n)}(dB(t_1), \dots, dB(t_n))
\end{aligned} \tag{8}$$

In such a case, the kernels can be also obtained by replacing expectation operation in the r.h.s. of (7) by the time average of the involved quantity.

III Structure of the time-invariant system and their wiener kernels

Some correspondence must exist between a system's physical structure and the system's kernels. Little is known, however, on the relationship. This is one of the reasons why Wiener's theory has not been very popular in system analysis. A list of kernels for each class of (analytically known) nonlinearities may help to abbreviate the problem[7]. The kernels also have to be reconciled with the traditional description of systems based on the block diagrams or a set of differential equations. Here we will discuss the cases where kernels were determined analytically.

(a) Linear system F_0

the white-noise input produces from a linear system, F_0 , with an impulse response function, $h(t)$, an output:

$$X(t; \omega) = \int_{-\infty}^t h(t-s) dB(s) \tag{9}$$

Thus, $X(t; \omega)$ is written by the first-order functional whose kernel is $h(-t)$. $X(t; \omega)$ is a Gaussian process with the mean 0. The correlation function is:

$$R(\tau) = \int_0^{\infty} h(t) h(t+\tau) dt$$

Conversely, a Gaussian process whose spectrum satisfies Paley-Wiener's condition is expressible in the form of (9). For instance, a linear system, say $F: d/dt$, without any impulse response function does not have the expression (9).

(b) Squarer device

Let F_2 be a squarer, a device which gives the output $X(t)^2$ to an input $X(t)$. Then the kernels of the cascade system of F_0 and F_2 are (Fig.1 a):

$$\begin{aligned} X(t; \omega) &= \left(\int_{-\infty}^t h(t-s) dB(s) \right)^2 \\ &= I_2(h(\cdot - t_1)h(\cdot - t_2), B(\cdot)) + \int_0^{\infty} h(t)^2 dt \end{aligned} \quad (10)$$

The system's second-order kernel is $h(-t_1)h(-t_2)$ and the 0th order kernel is:

$$\int_0^{\infty} h(t)^2 dt$$

(c) Nonlinear device without memory

Let F_N be a nonlinear device without memory in which an input, $X(t)$, produces the output, $y(x(t))$. Then the kernels of a cascade system of F_0 and F_N are (Fig.1b):

$$Y(t; \omega) = y\left(\int_{-\infty}^t h(t-s) dB(s) \right) \quad (11)$$

Let $X(t; \omega)$ be the output of F_0 . For a fixed but arbitrary t , $X(t; \omega)$ is subject to the Gaussian distribution with the mean 0 and the variance $\sigma^2 = \int_0^{\infty} h(t)^2 dt$.

If $y(X(t; \omega))$ is expanded by the Hermite polynomials:

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$$y(x(t; \omega)) = \sum_{n=0}^{\infty} d_n H_n\left(\frac{x(t)}{\sigma}\right) \quad (12)$$

where:

$$d_n = \frac{1}{\sqrt{2\pi\sigma n!}} \int_{-\infty}^{\infty} y(x) H_n\left(\frac{x}{\sigma}\right) e^{-\frac{x^2}{2\sigma^2}} dx \quad (13)$$

Now:

$$\begin{aligned} H_n\left(\frac{x(t)}{\sigma}\right) &= H_n\left(\frac{1}{\sigma} \int_{-\infty}^t h(t-s) dB(s)\right) \\ &= \frac{1}{\sigma^n} \int_{-\infty}^{\infty} \dots \int_{-\infty}^{\infty} h(t-s_1) \dots h(t-s_n) h^{(n)}(dB(s_1), \dots, dB(s_n)) \end{aligned}$$

Then, the n-th order kernel of $Y(t; \omega)$ is:

$$\frac{1}{\sigma^n} h(-t_1) \dots h(-t_n). \quad (14)$$

EX.1 For the case that $y(x)=1, x \geq 0; = -1, x \leq 0$:

$$d_{2n}=0, \quad d_{2n+1} = \sqrt{\frac{2}{\pi}} \frac{(-1)^n (2n-1)!!}{(2n+1)!} \quad (15)$$

Thus:

$$\begin{aligned} Y(t; \omega) &= \sqrt{\frac{2}{\pi}} \sum_{n=0}^{\infty} \frac{(-1)^n (2n-1)!!}{\sigma^{2n+1} (2n+1)!} \int_{-\infty}^t \dots \int_{-\infty}^t h(t-s_1) \dots h(t-s_n) x \\ &\quad x h^{(n)}(dB(s_1), \dots, dB(s_n)) \end{aligned} \quad (16)$$

The autocorrelation function of the output (16) is:

$$\begin{aligned} R_{YY}(\tau) &= EY(t; \omega)Y(t+\tau; \omega) - (EY(t; \omega))^2 \\ &= \sum_{n=1}^{\infty} \frac{n! d_n}{\sigma^{2n}} (R_{XX}(\tau))^n \end{aligned}$$

since $\sigma^2 = R_{xx}(0)$, we obtain:

$$R_{xx}(\tau) = \frac{2}{\pi} \arcsin\left(\frac{R_{xx}(\tau)}{R_{xx}(0)}\right)$$

This is the arcsine law for the clipped noise [18].

(d) Sandwich system

A sandwich system is composed of the system in (c) and a linear system with an impulse response function, $g(t)$ (Fig.2). The system's output is:

$$Z(t; \omega) = \int_{-\infty}^t g(t-s) Y\left(\int_{-\infty}^s h(s-\tau) dB(\tau)\right) ds \quad (17)$$

Using the expression of the output $Y(t; \omega)$ of F:

$$Z(t; \omega) = \sum_{n=0}^{\infty} \frac{d_n}{\sigma^n} \int_{-\infty}^t g(t-s) \int_{-\infty}^s h(s-\tau_1) \dots h(s-\tau_n) x^{(n)}(dB(\tau_1), \dots, dB(\tau_n))$$

Thus the n -th order kernel, $k_n(\tau_1, \dots, \tau_n)$, of the sandwich system is:

$$k_n(\tau_1, \dots, \tau_n) = \frac{d_n}{\sigma^n} \int_{-\infty}^{\min(\tau_1, \dots, \tau_n)} g(\tau) h(\tau_1 - \tau) \dots h(\tau_n - \tau) d\tau \quad (18)$$

Let the n -dimensional Fourier transform of k_n be \hat{k}_n , then:

$$\hat{k}_n(\gamma_1, \dots, \gamma_n) = \frac{d_n}{\sigma^n} \hat{h}(\gamma_1) \dots \hat{h}(\gamma_n) \hat{g}(\gamma_1 + \dots + \gamma_n) \quad (19)$$

where \hat{h} and \hat{g} are the Fourier transforms of h and g , respectively.

(f) Wiener kernels of systems described by Itô's stochastic

differential equations.

Here, Itô's stochastic differential equation is interpreted to describe the output of a dynamical system with the Gaussian white noise input. Our interest is on how the solution process (system's output) is expressed in terms of the Brownian functionals. Wiener kernels are known only in a few processes which are described by Ito's stochastic differential equation.

$$\text{EX.1} \quad dX(t) = aX(t)dt + (bX(t) + b')dB(t) \quad a \geq 0$$

Denote the kernels of $X(t)$ by $x_n(t_1, \dots, t_n)$, $n \geq 0$. Hida[14] showed that:

$$\begin{aligned} x_0 &= 0 \quad (\text{since } EX(t) = 0), \\ x_1(t_1) &= b \exp(-at), \quad t \geq 0; \quad 0, \quad t < 0 \\ x_n(t_1, \dots, t_n) &= (n!)^{-1} b^{n-1} b' \exp(-a \min_{1 \leq j \leq n} t_j) \phi_{(-\infty, 0]}^n(t_1, \dots, t_n) \end{aligned} \quad (20)$$

where: $\phi_{\Delta}^n(t_1, \dots, t_n) = \phi_{\Delta}(t_1) \dots \phi_{\Delta}(t_n)$. Here $\phi_{\Delta}(t)$ is the characteristic function of the interval Δ .

$$\text{EX.2} \quad dX(t) = f(t)X(t)dB(t)$$

The solution is expressed by McKean [19] as :

$$X(t) = \exp\left(\int_0^t f(s)dB(s) - \frac{1}{2} \|f\|_t^2\right), \quad \|f\|_t^2 = \int_0^t f(s)^2 ds \quad (21)$$

From the above equation, we have the expansion of $X(t; \omega)$ whose n th-order kernel is:

$$x_n(t_1, \dots, t_n) = \frac{1}{n!} f(t_1) \dots f(t_n) \quad (22)$$

EX.3 Itô's stochastic equation in general form.

We consider Itô's equation:

$$dX(t) = f(X)dt + g(X)dB(t), \quad X(0) = \xi_0 \quad (23)$$

where f and g satisfy some regularity conditions and the constant initial value ξ_0 is independent of $\{B(t), t > 0\}$. Then the solution $X(t)$ is a stationary Markov process and its kernels satisfy the following differential equations:

$$\begin{aligned} dx_0 &= f_0 dt \\ dx_n(t-t_1, \dots, t-t_n) &= f_n(t-t_1, \dots, t-t_n) dt \\ &+ \langle g_{n-1}(t-t_1, \dots, t-t_{n-1}) \phi_{(t, t+dt)}(t_n) \rangle \\ &n \geq 1 \end{aligned} \quad (24)$$

Hida solved the equations for the bilinear system to obtain the kernels[14].

Isobe and Sato found a formula to compute the kernels of the systems which were described by Itô's equation. Since the solution was Markovian, its transition p.d.f., $p(\xi, t | \xi', t')$, satisfied the Fokker-Planck equation[20].

$$\frac{\partial p}{\partial t} = - \frac{\partial f p}{\partial \xi} + \frac{1}{2} \frac{\partial g^2(\xi) p}{\partial \xi^2} \quad (25)$$

Then, the n th-order kernel $x_n(t_1, \dots, t_n; t)$ of $X(t)$ for a fixed but arbitrary t is:

$$\begin{aligned} x_n(t_1, \dots, t_n; t) &= (-1)^n \int_{-\infty}^{\infty} Q_n(t_1, \dots, t_n; t, \xi) d\xi \\ &t_1 < \dots < t_n < t \end{aligned} \quad (26)$$

where:

$$Q_n(t_1, \dots, t_n; t, \xi) = \int_{n\text{-fold}} \int P(\xi, t | \xi_n, t_n) \prod_{j=1}^n \frac{\partial P(\xi_j, t_j | \xi_{j-1}, t_{j-1}) g(\xi_j)}{\partial \xi_j} \times \\ \times d\xi_1 \dots d\xi_n \quad (27)$$

(g) Wiener kernels as a function of the power of the Gaussian white noise input (an integro-differential formula)

Let us consider a process $B_A(t) = \sqrt{A}B(t)$ (A ; positive constant) and call it as the Brownian motion, too. $B(t) = B_1(t)$ is then called as the standard Brownian motion for the distribution. Suppose that the system ψ receives the differential process $B_A(t)$ as the input. The output of the system ψ is then considered to be equivalent to that of the system ψ following an ideal preamplifier of gain \sqrt{A} to which the derivative of the standard Brownian motion $B(\cdot)$ is supplied instead of $B_A(\cdot)$.

$$Y(t) = \psi(B_A(\cdot)) = \psi(\sqrt{A} B(\cdot))$$

Then one can consider the Wiener expansion of the latter output. The kernels appearing in its orthogonal functional expansion are functions of the gain \sqrt{A} of the preamplifier: Isobe and Sato[21] derived the following relationship. Note that the over-all system's kernels depend on the input power A . Let us rewrite the kernels as

$$k_n(t_1, \dots, t_n; A) \quad n = 0, 1, 2, \dots$$

$$\frac{\partial}{\partial A} \left\{ \frac{k_n(t_1, \dots, t_n; A)}{A^{\frac{n}{2}}} \right\} = \frac{\binom{n+2}{2}}{A^{\frac{n+2}{2}}} \int_{-\infty}^{\infty} k_{n+2}(t_1, \dots, t_n, \tau, \tau; A) d\tau$$

(28)

$$\frac{\partial^m}{\partial A^m} \left\{ \frac{k_n(t_1, \dots, t_n; A)}{A^{\frac{n}{2}}} \right\} = \frac{(n+2m)!}{2^m n! A^{\frac{n+2}{2}}} \times \\ \times \int_{-\infty}^{\infty} \dots \int_{-\infty}^{\infty} k_{n+2m}(t_1, \dots, t_n, \tau_1, \tau_1, \dots, \tau_m, \tau_m; A) d\tau_1 \dots d\tau_m$$

The kernels of a system ψ are obviously:

$$\{k_n(t_1, \dots, t_n; 1)\}.$$

EX. Sandwich system

Isobe and Sato[21] applied the results discussed above to the sandwich system as shown in Fig.2 and obtained a relationship:

$$\frac{d^n c_n(A)}{dA^n \frac{n}{A^2}} = \binom{n+2}{2} \frac{c_{n+2}(A)}{A^{\frac{n+2}{2}}} \quad (29)$$

Thus we obtain $\{c_n(A)\}$ from $c_0(A)$ and $c_1(A)$ via formula (29). Here we have:

$$y(\sqrt{A}x) = \sum_{n=0}^{\infty} c_n(A) H_n(x) \quad (30)$$

$$c_n(A) = \frac{1}{2\pi n!} \int_{-\infty}^{\infty} y(\sqrt{A}x) e^{-\frac{x^2}{2}} dx$$

Thus a sandwich system is identified by measuring the kernels up to the second-order at most. In fact, Isobe and Sato [21] showed that $h(t)$, $g(t)$ and $y(x)$ could be determined from the kernels obtained with the Gaussian white noise inputs of different power.

IV Biological applications

In the past decade, the theory has seen a number of practical applications in biological systems' analysis, particularly in the vertebrate visual system. As would be expected from any pioneering effort, many errors, theoretical as well as practical, have been made in the process and, more important, as many theoretical developments and ingenious technical improvements have been made[5]. In this

section, we will discuss the neural network analysis in the vertebrate retina which is one of the few biological preparations in which Wiener's analytical method has been extensively applied[22]. In untangling the circuitry in the retina, white-noise modulated test current can be injected into one neuron and resulting responses can be recorded from other neurons. By cross-correlating the input with the output, one defines the transfer function between the two neurons. If the transmission is (quasi) linear, the first-order kernel is the impulse response of the system: if the transmission is nonlinear, higher order kernels will describe the deviation from the linear transmission. In Fig. 3 are shown results of current-injection experiment in which white-noise modulated current (flat power from near dc to 50HZ with zero mean) was injected into one horizontal cell and resulting response was recorded from another horizontal cell located about 400 microns away. the power spectra of the injected current and potential changes registered by the second electrode matched almost exactly, i.e., the system (current flow between two horizontal cells) could respond to much faster input. (Such input could not be used from some technical difficulties.) The spread of current among the cells was quasi-linear as we expected from the fact that the cells formed a lamina. By Fourier transforming the first order kernel, one obtains the gain and phase of the transmission was constant to indicate that the horizontal cells formed a constant-gain lowpass filter. On the other hand, the transmission from horizontal to amacrine cells has large second-order nonlinear component depicted in the second-order Wiener kernel shown in Fig.4.

Despite obvious advantages as mentioned in the first section, its practical applications made so far have not been an unqualified success. The difficulties arise from several factors; 1) Interpretation of higher order kernels is problematic. With a few exceptions, one of which is the 'sandwich system', there is no formal correspondence between a system's physical structure and kernels. 2) In many cases, the relationship between the input, white-noise signals, and the output, resulting neural responses, can not be seen intuitively. The relationship can only be obtained by computing kernels, a process difficult to perform 'on-line'. Often it is not possible to draw preliminary conclusions during experiments or to modify them observing the results of on-going experiment. 3) A comprehensive computing system is a prerequisite for an efficient white-noise analysis. The difficulties, however, are not insurmountable, theoretically or technically and they may be dissolved through future efforts.

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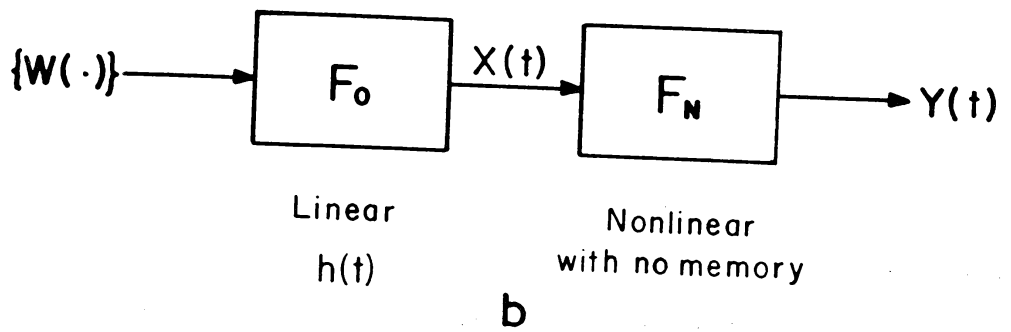
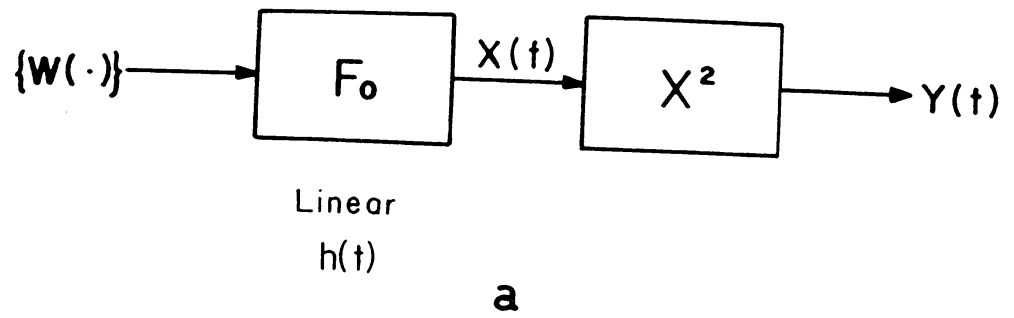


Fig.1 a; Squarer device following a linear system with impulse response function $h(t)$
 b; Memoryless nonlinear device following a linear system $h(t)$

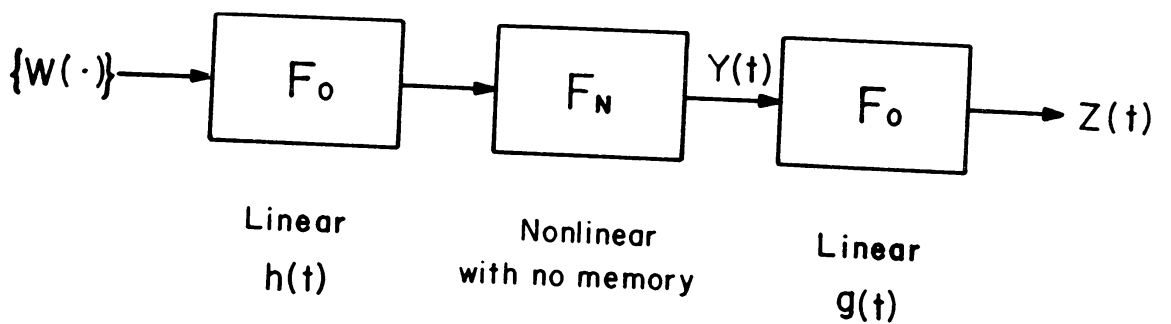


Fig.2; Sandwich system

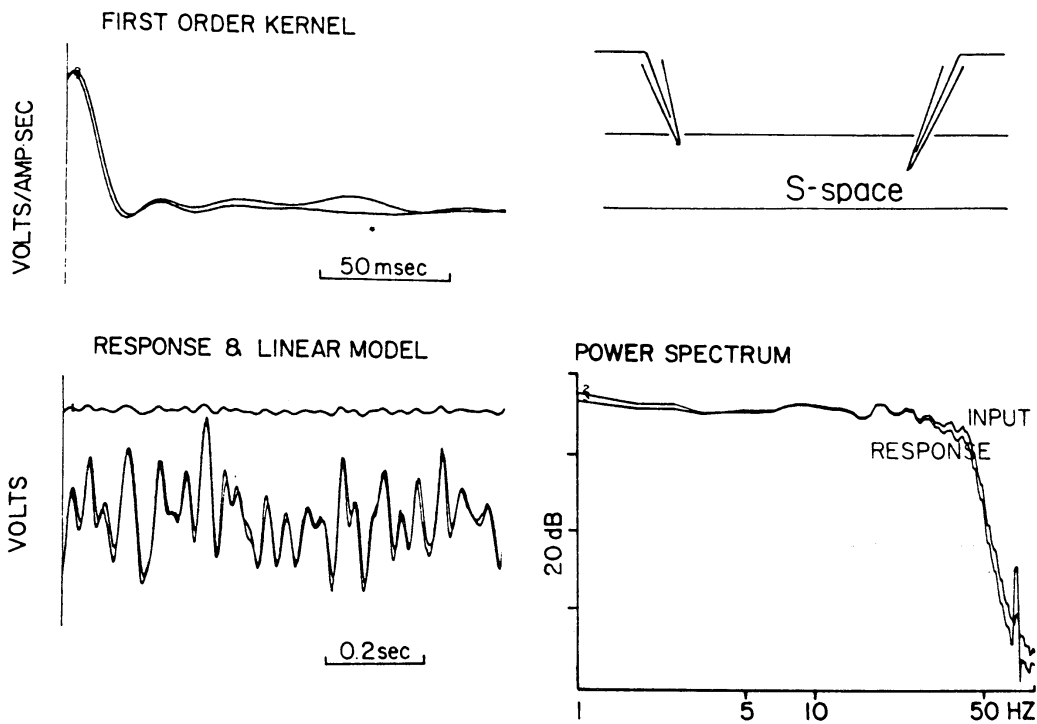


Fig.3; Current injection experiment on a retinal system and the first order kernels. See the text for details.

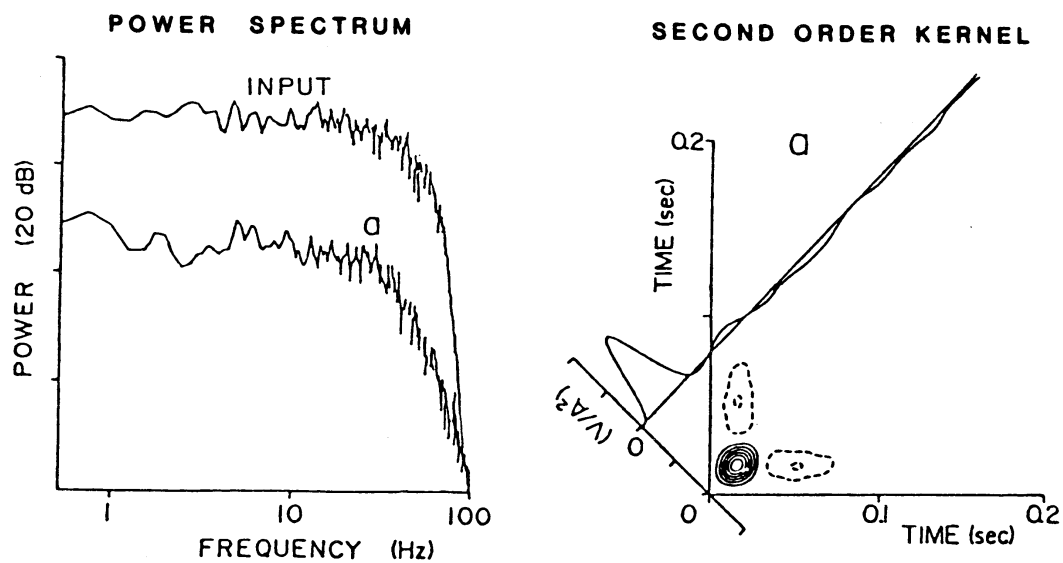


Fig.4; Examples of the second order kernel