



## **A NEW BIO MATHEMATICAL MODEL TO ESTIMATE THE EFFECT OF H<sub>2</sub>O<sub>2</sub> AND EGF BY USING STOCHASTIC DIFFERENTIAL EQUATIONS**

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### **Abstract:**

*Hydrogen Peroxide (H<sub>2</sub>O<sub>2</sub>) and Epidermal Growth Factor (EGF) activate phosphatidylinositol 3-kinase and increase sodium transport in A6 cell monolayers. Activation of phosphatidylinositol 3-kinase (PI 3-kinase) is required for insulin stimulation of sodium transport in A6 cell monolayers. In this study, we estimate the effect of hydrogen peroxide (h<sub>2</sub>o<sub>2</sub>) and epidermal growth factor (EGF) by using stochastic differential equations.*

**Key Words:** Hydrogen Peroxide, Epidermal Growth Factor, PI3-Kinase, Stochastic Differential Equations & Normal Distribution

### **Introduction:**

Epidermal growth factor (EGF) and hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) are known activators of PI3-kinase in several systems. However, EGF appears to affect sodium transport quite variously: it increases sodium absorption in the airways and in the intestine, whereas it inhibits sodium absorption in a murine collecting tubule cell line (mCT1), in rabbit collecting tubules, and in a C7 clone of Madin-Darby canine kidney (MDCK) cells. Thus the action of EGF appears quite specific to the cells involved. In renal cells, the observed decrease in sodium transport was suggested to result from activation of the mitogen activated protein kinase (MAPK) signaling pathway, whereas the enhanced sodium absorption observed in the intestine was attributed to the activation of a brush border PI3-kinase [6].

This paper introduces the survey of numerical solution methods for stochastic differential equations. The solution will be continuous stochastic processes that represent diffusion dynamics. We include a review of fundamental concepts, a description of elementary numerical methods and the concepts of convergence and order for stochastic differential equation solvers. The Euler Maruyama method to the Black scholes stochastic differential equations.

$$w_{i+1} = w_i + \mu w_i \Delta t_i + \sigma w_i \Delta W_i$$

### **Stochastic Differential Equations:**

Unlike deterministic models, ordinary differential equations of which have a unique solution for much appropriate initial condition, SDE's have solutions that are continuous - time stochastic processes. Methods for the computational solution of stochastic differential equation are based on similar techniques for ordinary differential equations.

We will begin with a quick survey of the most fundamental concepts from stochastic calculus that are needed to proceed with our description of numerical methods. For full details, the reader may consult [4] [7] & [9].

A set of random variables  $X_t$  indexed by real numbers  $t \geq 0$  is called a continuous-time stochastic process. Each instance, of the stochastic process is a choice from the random variable  $X_t$  for each  $t$ .

Any (deterministic) function  $f(t)$  can be trivially considered as a stochastic process, with variance  $V(f(t)) = 0$ . Here the Wiener process  $w_t$ , a continuous-time stochastic process with the following three properties.

**Property 1:** For each  $t$ , the random variable  $W_t$  normally distributed with mean 0 and variance  $t$ .

**Property 2:** For each  $t_1 < t_2$ , the normal random variable  $W_{t_2} - W_{t_1}$  is independent of the random variable  $w_t$  and is fact independent of all  $W_t, 0 \leq t \leq t_1$

**Property 3:** The Wiener process  $w_t$  can be represented by continuous paths.

A typical diffusion process is modeled as a differential equation involving deterministic and stochastic, the latter represented by a Wiener process, as in the equation

$$dX = a(t, X) dt + b(t, X) dW_t \tag{1}$$

The SDE (1) is given in a differential form, unlike the derivative form of an ODE. That is because many interesting stochastic processes, like Brownian motion, are continuous but not differentiable. Therefore the meaning of the SDE (1) is by definition, the integral equation

$$X(t) = X(0) + \int_0^t a(s, y) ds + \int_0^t b(s, y) dW_s$$

Where the meaning of the last integral, called an Ito integral.

Let  $c = t_0 < t_1 \dots < t_{n-1} < t_n = d$  be a grid of points on the interval  $[c, d]$ .

The Riemann integral is defined as a limit  $\int_c^d f(x) dx = \lim_{\Delta t \rightarrow 0} \sum_{i=1}^n f(t'_i) \Delta t_i$ ,

Where  $\Delta t_i = t_i - t_{i-1}$  and  $t_{i-1} \leq t'_i \leq t_i$ .

Similarly, the Ito integral is the limit  $\int_c^d f(t) dW_t = \lim_{\Delta t \rightarrow 0} \sum_{i=1}^n f(t_{i-1}) \Delta W_i$

Where  $\Delta W_i = W_{t_i} - W_{t_{i-1}}$  a step of Brownian motion across the interval.

Because  $f$  and  $W_t$  are random variables, so is the Ito integral  $I = \int_c^d f(t) dW_t$ . The

differential  $dI$  is a notational convenience; thus  $I = \int_c^d f dW_t$

is expressed in differential form as  $dI = f dW_t$

To solve SDEs analytically, we need to introduce the chain rule for stochastic differentials, called the Ito formula [8].

If  $Y = f(t, X)$ , then  $dY = \frac{\partial f}{\partial t}(t, X) dt + \frac{\partial f}{\partial x}(t, X) dx + \frac{1}{2} \frac{\partial^2 f}{\partial x^2}(t, X) dx dx$  (2)

Where the  $dx dx$  term is interpreted by using the identities

$$\begin{aligned} dt dt &= 0 \\ dt dW_t &= dW_t dt = 0 \\ dW_t dW_t &= dt \end{aligned} \tag{3}$$

The Ito formula is the stochastic analogue to the chain rule of conventional calculus. The important features of typical stochastic differential equations can be illustrated using the Black Scholes diffusion equation [1] [2] & [3].

$$\begin{aligned} dX &= \mu X dt + \sigma X dW_t \\ X(0) &= X_0 \end{aligned} \tag{4}$$

The solution of the Black Scholes stochastic differential equation is geometric Brownian motion

$$X(t) = X_0 e^{(\mu - \frac{1}{2}\sigma^2)t + \sigma W_t} \tag{5}$$

To check this, write  $X = f(t, Y) = X_0 e^Y$ , where  $Y = (\mu - \frac{1}{2}\sigma^2)t + \sigma W_t$ . By the Ito formula,

$$dX = X_0 e^Y dY + \frac{1}{2} e^Y dY^2$$

Where  $dY = (\mu - \frac{1}{2}\sigma^2)dt + \sigma dW_t$ . Using the differential identities from the Ito formula [2] & [3]

$$dY dY = \sigma^2 dt$$

And therefore

$$\begin{aligned} dX &= X_0 e^Y (\mu - \frac{1}{2}\sigma^2)dt + X_0 e^Y \sigma dW_t + \frac{1}{2} \sigma^2 e^Y dt \\ &= X_0 e^Y \mu dt + X_0 e^Y \sigma dW_t \\ &= \mu X dt + \sigma X dW_t \end{aligned}$$

as claimed.

**Numerical Methods for SDEs:**

The Euler Maruyama method is the analogue of the Euler method for ordinary differential equations [5] & [8]. To develop an approximate solution on the interval  $[c, d]$ , assign a grid of points  $c = t_0 < t_1 < t_2 < \dots < t_n = d$

Approximate  $x$  values  $\omega_0 < \omega_1 < \omega_2 < \dots < \omega_n$  will be determined at the respective  $t$  points. Given the SDE initial value problem

$$\begin{aligned} dX(t) &= a(t, x)dt + b(t, x)dW_t \\ x(c) &= X_c \end{aligned} \tag{6}$$

We compute the approximate solution as follows:

**Euler - Maruyama Method:**

$$\begin{aligned} \omega_0 &= X_0 \\ \omega_{i+1} &= \omega_i + a(t_i, \omega_i)\Delta t_{i+1} + b(t_i, \omega_i)\Delta W_{i+1} \end{aligned} \tag{7}$$

Where  $\Delta t_{i+1} = t_{i+1} - t_i$  &  $\Delta W_{i+1} = W(t_{i+1}) - W(t_i)$  (8)

Define  $N(0,1)$  to be the standard random variable that is normally distributed with mean 0 and standard deviation 1. Each random number  $\Delta W_i$  is computed [10], where  $z_i$  is chosen from  $N(0, 1)$ . Each set of  $\{\omega_0, \dots, \omega_n\}$  produced by the Euler Maruyama method is an approximate realization of the solution stochastic process  $X(t)$  which depends on the random numbers  $Z_i$  that were chosen.

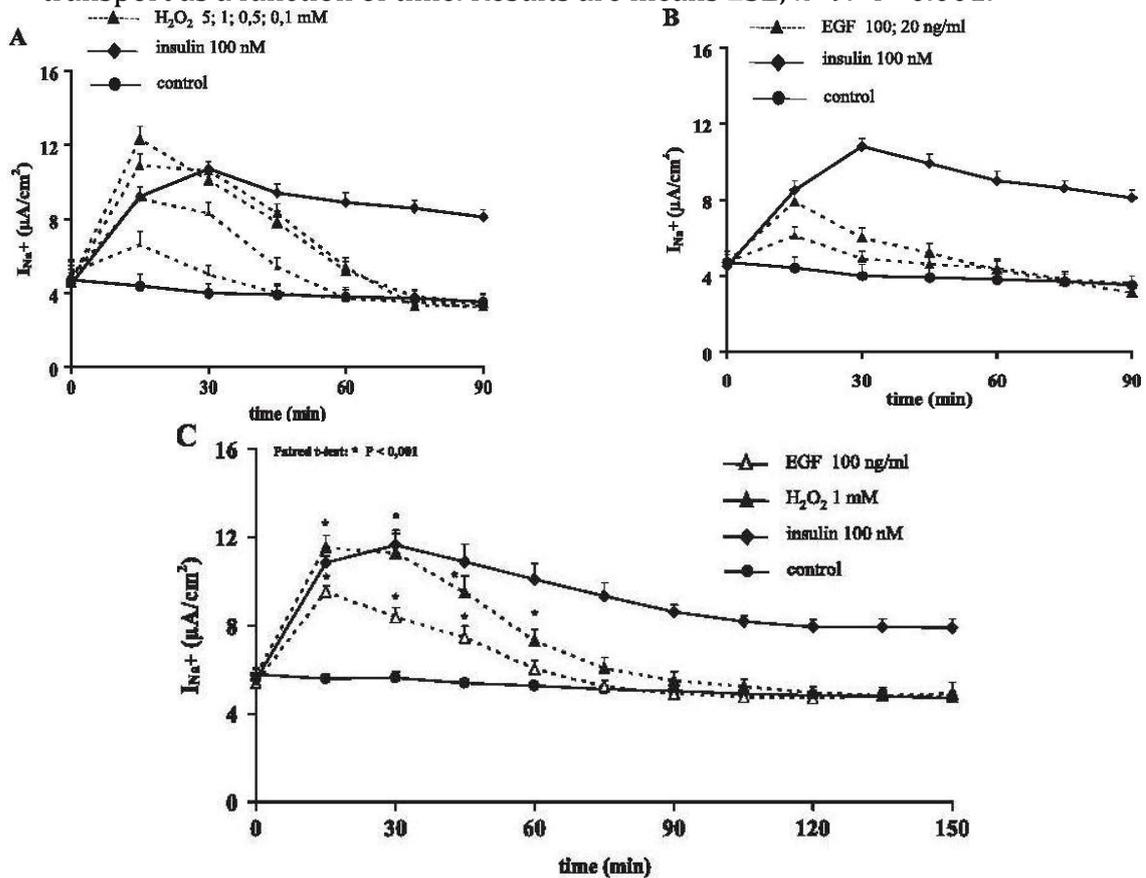
The Euler Maruyama equations (7) to the Black Scholes SDE (4) have form

$$\begin{aligned} w_0 &= X_0 \\ w_{i+1} &= w_i + \mu w_i \Delta t_i + \sigma w_i \Delta W_i \end{aligned} \tag{9}$$

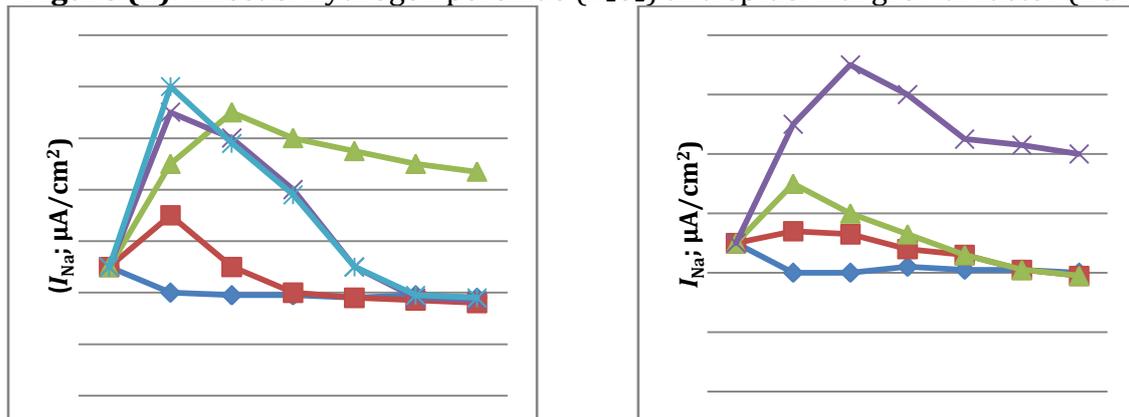
**Example:**

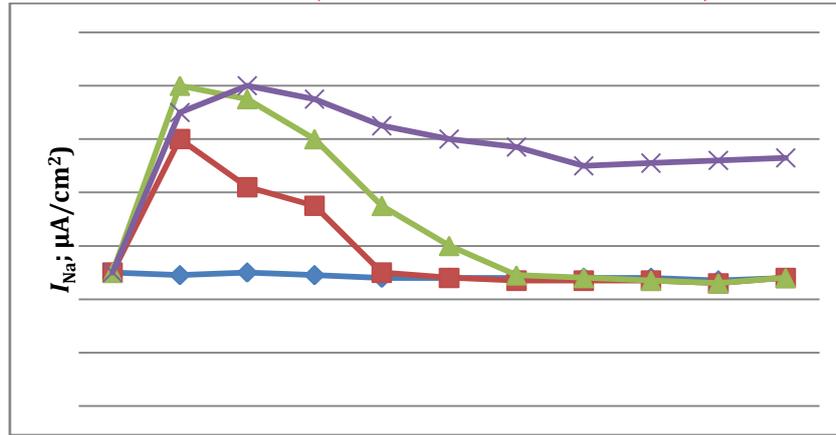
Effect of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and epidermal growth factor (EGF) on sodium transport across A6 cell monolayers. The increase in sodium transport ( $I_{Na^+}$ ; measured in  $\mu A/cm^2$ ) induced by H<sub>2</sub>O<sub>2</sub> and EGF was compared with that induced by insulin (100 nM, basolateral).

- Addition of H<sub>2</sub>O<sub>2</sub> into the apical bathing medium induced a concentration dependent increase in sodium transport with a maximal effect observed at 1 mM, after 15-30 min.
- Addition of EGF into the basolateral bathing medium induced a transient concentration dependent increase in sodium transport, with a maximum after 15 min. Values are means  $\pm$ SE;  $n=3$ .
- Summary of the effect of maximal doses of H<sub>2</sub>O<sub>2</sub>, EGF, and insulin on sodium transport as a function of time. Results are means  $\pm$ SE;  $n=9$ . \* $P<0.001$ .



**Figure (1):** Effect of hydrogen peroxide (h<sub>2</sub>o<sub>2</sub>) and epidermal growth factor (EGF)





**Figure (2):** Effect of hydrogen peroxide ( $H_2O_2$ ) and epidermal growth factor (EGF) by using Normal Distribution

**Conclusion:**

The Bio Mathematical Model also give the same cumulative effects of hydrogen peroxide ( $H_2O_2$ ) and epidermal growth factor (EGF) which are beautifully fitted with Euler –Maruyama method to the Black Scholes SDE. The medical reports are beautifully fitted with the mathematical model. Hence the mathematical report {Figure (2)} is coincide with the medical report {Figure (1)}.

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