A STOCHASTIC MODEL BY THE BIRTH AND DEATH PROCESS OF IRREDUCIBLE STATIONARY PROBABILITIES FOR THE GLP-1.

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Abstract: The Glucagon-like peptide-1 (GLP-1) inhibits appetite in part through regulation of soluble leptin receptors. GLP-1 is an incretin that it has the ability to decrease blood sugar levels in a glucose-dependent manner by enhancing the secretion of insulin. The time period of during weight loss maintenance, GLP-1 receptor agonist (GLP-1RA) administration may inhibits weight loss-induced increases in soluble leptin receptors there by preserving free leptin levels and preventing weight regain.

Here we develop a model for the customers arrive to the service according to a Poisson process of intensity λ and they immediately go to a free shop assistant, where they are received according to an exponential distribution of parameter μ.

$$p_k = \frac{1}{k!} e^{-\delta} \delta^k, k \epsilon N_0$$

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I. INTRODUCTION

GLP-1 is a hormone secreted from the endocrine L cells in the intestine, which reduces food intake and when administered to obese subjects, induces weights loss. (Astrup, A., Rössner, S., ,2009). It is well established that GLP-1 inhibits food intake by inhibiting appetite. However, the leptin receptor may be involved in the appetite inhibition by GLP-1. (Iepsen, E. W., 2015) Many obese people have a history of several successful weight losses, but very few are able to maintain the weight loss over a longer period of time. After weight loss, several physiological mechanisms favoring weight regain are activated, including declining energy expenditure in combination with hunger and reduced satiety during eating, (Rosenbaum, M.,2008) Here it has been hypothesized that the reduction in free circulating leptin after weight loss is responsible for the weight regain and experiments have shown that leptin repletion after weight loss can reduce weight regain by decreasing energy intake.

II. NOTATIONS

$\frac{1}{\lambda} - mean\ inter\ arrival\ time$
$\frac{1}{\mu} - mean\ service\ time$
$\lambda_k -$ Birth intensity at state E_k
$\mu_k -$ Death intensity at state E_k

III. BIRTH AND DEATH PROCESSES

Let $\{x(t)|t \in [0, D]\}$ be a stochastic process, which can be in the states $E_0, E_1, E_2, ...$ The process can only move from one state to a neighboring state in the following sense. If the process is in state E_k, and we receive a positive signal then the process is transferred to E_{k+1}, and if instead we receive a negative signal (and $k \in N$), then the process is transferred to E_{k-1}. (Lawler, G. F. 2018)

We assume that there are non-negative constants λ_k and μ_k, such that for $k \in N$,

1) $P\{one\ positive\ signal\ is\ ]\ t, t+h\ [\ |x(t) = k\}$
$= \lambda_k h + \lambda \in (h).$
2) $P\{one\ negative\ signal\ is\ ]\ t, t+h\ [\ |x(t) = k\}$

$= \mu_k h + h \in (h).$

3) $P\{no\ signal\ is\ ]\ t, t+h\ [\ |x(t) = k\}$

$= 1 - (\lambda_k + \mu_k)h + h \in (h),$

λ_k the birth intensity at state E_k, and μ_k is called the death intensity at state E_k, and the process itself is called a birth and death process. If in particular all $\mu_k = 0$, if it is a birth process, and a death process, if all $\lambda_k = 0$. (Mejlbro, L. 2009) (Medhi, J. 2002)

A simple analysis shows for $k \in N$ and $h > 0$ that the event $\{X(t+h) = k\}$ is realized in one of the following ways:

$X(t) = k$, and no signal in $]t, t+h[$.

$X(t) = k-1$, and one positive signal in $]t, t+h[$.

$X(t) = k+1$, and one negative signal in $]t, t+h[$.

More signals in $]t, t+h[$.

We put $P_k(t) = p\{X(t) = k\}$ (3.1)

By a rearrangement and taking the limit $h \to 0$, we easily derive the differential equation of the process,

$p_0'(t) = -\lambda_0 p_0(t) + \mu_1 p_1(t)$ for $k = 0$

$p_k'(t) = -(\lambda_k + \mu_k)\, p_k(t) + \lambda_{k-1} p_{k-1}(t) + \mu_{k+1} p_{k+1}(t)$, for $k \epsilon N$ (3.2)

In a special case of a pure birth process, where all $\mu_k = 0$, this systems is reduced to

$p_0'(t) = -\lambda_0 p_0(t)$ for $k = 0$

$p_k'(t) = -\lambda_k\, p_k(t) + \lambda_{k-1} p_{k-1}(t)$, for $k \epsilon N$ (3.3)

If all $\lambda_k > 0$, we get the following iteration formula of the complete solution,

$p_0(t) = C_0 e^{-\lambda_0 t}$, for k =0

$p_k(t) = \lambda_{k-1} e^{-\lambda_k t} \int_0^t e^{\lambda_k T} p_{k-1}(T) dT + C_k e^{-\lambda_k t} for\ K \epsilon N.$ (3.4)

Let $\{X(t), t\epsilon[0, +\infty]\}$ be a birth and death process, where all $\lambda_k and\ \mu_k$ are positive, with the exception of $\mu_0 and\ \lambda_N = 0$, if there is a final state E_N. The process can be in any of the states, therefore, in analogy with the markov chain, such a birth and death process is called irreducible. (H, Constantin, 2016)

In Queuing theory, if there exists a state E_k, in which $\lambda_k = \mu_k$, then E_k is an absorbing state, because it is not possible to move away from E_k.

For the most common birth and death processes there exist non-negative constants p_k, such that $p_k(t) \to p_k$ and

$p_k'(t) \to v,\ for\ t \to \infty.$

There constants fulfill the infinite system of equation,

$\mu_{k+1} p_{k+1} = \lambda_k p_k$, for $k \epsilon N_0$,

which sometimes can be used to find the p_k.

If there is a solution (p_k), which satisfies,

$p_k \geq 0$ for all $k \epsilon N_0$,

and $\sum_{k=0}^{\infty} p_k = 1$

The solution (p_k) is a stationary distribution, and the p_k are called the stationary probabilities.

In this case we have

$p_k(t) \to p_k\ for\ t \to \infty.$

If $\{X(t)|\ t \epsilon\ [0, \infty\ [$ is an irreducible process, then

$$p_k = \frac{\lambda_{k-1}\lambda_{k-2}\cdots\lambda_1\lambda_0}{\mu_k\mu_{k-1}\cdots\mu_2\mu_1} \cdot p_0 \tag{3.5}$$

where all $a_k > 0$.

The condition of the existence of a stationary distribution is then reduced to that the series $\sum_k a_k$ is convergent of finite sum $a > 0$.

In this case we have $P_0 = \frac{1}{a}$

IV. QUEUING PROCESSES

In the $M|M|1$ model is a poisson-input, exponential service, single server queue. The density functions for the inter arrival and service times are given. (Gross, D. 2008)

$$a(t) = \lambda e^{-\lambda t}$$

$$b(t) = \mu e^{-\mu t},$$

where ${}^{1}/_{\lambda}$ is the mean inter arrival time and ${}^{1}/_{\mu}$ is the mean service time.

Both the inter arrival and service time are exponential, and the arrival and conditional service rates are poisson, which gets us

$$p\{an\ arrival\ occurs\ is\ an\ inteval\ of\ length\ \Delta t\} = \lambda\Delta t + 0\ (\Delta t)$$

$$p\{more\ than\ one\ arrival\ occurs\ in\ \Delta t\} = 0\ (\Delta t)$$

$$p\{a\ service\ completion\ in\ \Delta t\ given\ the\ system\ is\ not\ empty\} = \mu\Delta t + 0\ (\Delta t)$$

$$p\{more\ than\ one\ service\ completion\ in\ \Delta t\ given\ more\ then\ one\ in\ the\ system\} = 0\ (\Delta t)$$

The $M|M|1$ model is a simple birth-death process with $\lambda_n = \lambda\ and\ \mu_n = \mu$ for all n.

Arrivals are 'births' to the system, since if the system is in state n (the state refers to the numbers of customers in the system), an arrival increases it to state $n + 1$.

Similarly, departures are death moving from state n to state $n - 1$.

Hence, the steady state equation are found to be

$$0 = -(\lambda + \mu)\,p_n + \mu p_{n+1} + \lambda p_{n-1}.$$

$$0 = -\lambda p_0 + \mu p_1$$

(or)

$$p_{n+1} = \frac{\lambda+\mu}{\mu}\,p_n - \frac{\lambda}{\mu}p_{n-1}$$

$p_1 = \frac{\lambda}{\mu}p_0$, which is a set of second order difference equation with constant coefficient.

To solve the steady state difference equation for $\{p_n\}$ using the iterative method since the $M|M|1$ systems is a birth-death process with constant birth and death rates, we have

$$p_n = p_0 \prod_{i=1}^{n} \frac{\lambda}{\mu}$$

$$= p_0 \left(\frac{\lambda}{\mu}\right)^n$$

To find p_0, we remember that probabilities must sum to 1 and it follows that

$$1 = \sum_{n=0}^{\infty} \left(\frac{\lambda}{\mu}\right)^n p_0$$

If $p = \frac{\lambda}{\mu}$ as the traffic intensity for the single-server queues.

$$p_0 = \frac{1}{\sum_{n=0}^{\infty} \rho^n}$$

Now $\sum_{n=0}^{\infty} \rho^n$is an infinite geometric series which converges if and only if $\rho < 1$

Thus, the only way for a steady-state solution to exist, if and only if $\rho < 1$

Since, we know the sum of the terms of a convergent geometric series

$$\sum_{n=0}^{\infty} \rho^n = \frac{1}{1-\rho} \ (\rho < 1)$$

We find $p_0 = 1 - \rho$, which confirms the general results for p_0 we derived in the $G|G|1$.

Thus the full steady-state solution for the $M|M|1$ systems in the geometric probability function.

$$p_n = (1-\rho)\rho^n \left(\rho = \frac{\lambda}{\mu} < 1\right)$$

The stochastic process is described by the birth and death process,

$\{\alpha(t)/t \in [0, +\infty[\}$ and $\lambda_k = \lambda \ and \ \mu_k = k\mu$ for all k.

The process is irreducible, and the differential equation of the system are given by

$p_0'(t) = -\lambda p_0(t) + \mu p_1(t)$ for k=0

$$p_k'(t) = -(\lambda + k\mu)p_k(t) + \lambda p_{k-1}(t) + (k+1)\mu p_{k+1}(t) \text{ for } k\epsilon N \quad (4.1)$$

The stationary probabilities exist and satisfy the equations

$(k+1)\mu p_{k+1} = \lambda p_k, k\epsilon N_0$ of the solutions

$$p_k = \frac{1}{k!}(\delta)^k e^{-\delta}, k\epsilon N_0 \quad (4.2)$$

These are the probabilities that there are k customers in the system, when we have obtained equilibrium. The results of the Fig.2 are applied in the Eq. 4.2 are shown in Fig. 1. (Kumar, P. S., & Sundari, D. S. .2014) (Senthilkumar, P., & Sundari, D. S. 2015)

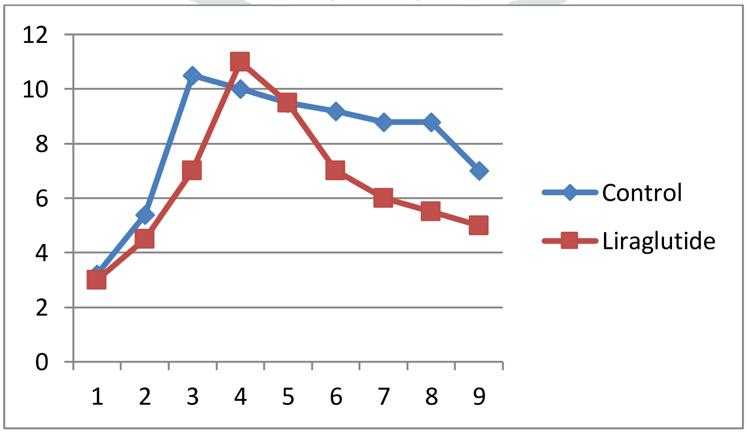

Figure 1 Endogeneous GLP-1 in Control and Liragultide by irreducible stationary probabilities.

V. EXAMPLE

Each study participant underwent three meal tests, at screening, after 8 weeks on very low calorie powder diet, and after 52 weeks with restrictive weight maintenance diet and recommendations (Astrup, A., Rössner, S., ,2009). Various blood samples for measurements of Endogenous GLP-1 were taken before the intake of Fresutrin energy drink and every 15 min until 180 min after meal ingestion. (Kissileff, H. R.,2008) The 12% weight loss was successfully maintained in both the groups with no significant difference in weight between the beginnings of the weight loss maintenance program to after 52 weeks. In endogenous GLP-1 levels were significantly lower in the GLP-1RA group compared with the control group.

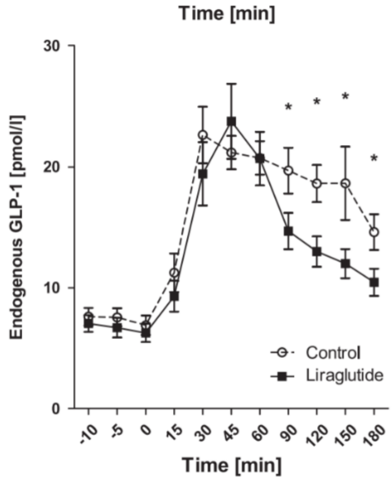

Figure 2 – Endogeneous GLP-1 in Control and Liragultide

VI. CONCLUSION

The mathematical model also reflects the same effects in the endogenous GLP-1, levels were lower in the GLP-1RA group compared with the control groups (fig 2) which are beautifully fitted with birth and death processes of irreducible stationary probabilities fig (1). The results matching with the mathematical and medical report.

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