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A MATHEMATICAL MODEL FOR INSULIN RECEPTOR SIGNALING IN THE GNRH NEURON PLAYS A ROLE IN THE ABNORMAL GNRH PULSATILITY OF OBESE FEMALE MICE

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Abstract. In the present paper a generalized Birth and Death process as model for degradation and aging process for biological objects is proposed. Obese control female mice were infertile with higher luteinizing hormone levels and higher GnRH pulse amplitude and total pulsatile secretion compared to learn control mice. The variation of the model parameters allows to consider various problems of aging and degradation control application part illustrate our approach. Finally ,we conclude that the application part coincides with a mathematical model and result is linked to the medical report. In the future, this paper will be very beneficial in the medicinal field.

1. Introduction

Let us consider a structure with only three states, which can be treated as an example of the model of aggregated states, where all the states of each group are working normally N. Degradation D is fused into one and deficiency F. For convenience, assume that the loss happens in line with the Poison flow [6, 7, 8, 9]. But repair times are normally distributed with the cumulative distribution function $B(x)$ and the hazard rate $\alpha(x)$.

2. Mathematical model and assumptions

In accordance with given transition graph the Kolmogorov's system of differential equations for system states probabilities has the form

$$\begin{aligned} u\pi_m(s)/ds &= -(\lambda+\gamma)\pi_m(t) + \int_0^t \alpha(y)\pi_u(s,y)dy \\ \frac{\phi\Pi U(s)}{\phi(s)} + \frac{\phi\Pi U(s,y)}{\phi(y)} &= -(w+\alpha(y))\pi M(S,Y) \\ U\pi_E(s)/ds &= \beta\pi_M(s) + w\pi U(s,y) \end{aligned} \tag{2.1}$$

With the initial and boundary condition

$$\begin{aligned} \pi_u(s,y) &= \mu\pi U(s) \\ \Pi_M(0) = 1, \qquad \pi_u(0,0) &= \pi_E(0) = 0 \end{aligned} \tag{2.2}$$

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The reliability function of the system is

$$P(s) = 1 - \pi E(s) = 1 - \int_0^s \beta\pi M(v) + v\pi D(v)dv \tag{2.3}$$

Where the functions $\pi_M(s)$ and $\pi_U(s,r)$ are the solutions of the first two equations of the system (2.1) and

$$\Pi_U(s) = \int_0^s \pi_u(s,y)dy \tag{2.4}$$

The solution of the second equation from the system (2.1) accordingly.

$$\Pi_i(s,y) = f_i(s-y)(1-X_i(y))(1-Y_i(y)), \quad 0 \le y \le s < \infty, i \in E$$

can be given in the form

$$\Pi_U(s,y) = \pi(s-y)e^{-uy}(1-Y(y)) \tag{2.5}$$

Where the function $g_D(t)$ is determined from the boundary condition (2.2). It gives

$$\Pi_U(s,y) = \lambda\pi M(s-y)e^{-ux}(1-Y(y))$$

Substitution of this solution into the first equation of the system (2.1) gives the following equation.

$$u\pi_M(t)/ds = -(\lambda+\gamma)\pi_M(s) + \lambda\int_0^t \alpha(y)\pi_M(s-y)ye^{-wy}(1-Y(y)dy \tag{2.6}$$

The best method for its solution is a LT approach. In the terms of LT with the initial condition (2.2) and equation (2.6) after the usual order of integration changing takes the form

$$P\pi^{M(t)} - 1 = -(\lambda+\gamma)\pi^{M(t)} + \lambda\alpha^{t+w}\pi^{N(t)}$$

where $\alpha^s = \int_0^s e^{-ts}\alpha(y)dy$ is a LT of the probability density function $\alpha(y)$.It Follows from here that the solution of the last equation has a form

$$\pi^{M(t)} = [t+\gamma+\lambda(1-\alpha^{(t+w)})]^{-1} \tag{2.7}$$

Next, the conclusion of the LT $\pi^{U(t)}$ of the function $\pi U(t)$ given by equation (2.4) after substitution in to of the expression (2.7)) gives

$$\begin{aligned}\pi^{U(t)} &= \int_0^s e^{-st}\int_0^s \pi U(s,y)dyds = \int_0^t\int_0^t \lambda\pi M(s-y)e^{-wy}(1-A(y))dyds \\ &= \frac{\lambda\pi^{M(u)}(1-\alpha^{(t+w)})}{t+w} = \frac{\lambda(1-\alpha^{(t+w)})}{(t+w)(t+x)+\lambda(1-\alpha^{(t+w)})}\end{aligned} \tag{2.8}$$

At least for the LT $\pi^{E(s)}$ of the function $\pi E(t)$ from the last equations (2.1) one can find

$$T\pi^{E(t)} = \gamma\pi^{M(t)} + w\pi^{U(t)} = \frac{\gamma(t+w)+\lambda w(1-\alpha^{(t+w)})}{(t+w)(t+\gamma+\lambda(1-\alpha^{(t+w)})} \tag{2.9}$$

Therefore for the LT of the reliability function (2.3) we get the mean lifetime of the object can be found from the last expression For the measurement of the limiting values of the probabilities of conditional state on lifetime [5, 10, 11, 12,

13, 14]. We use the above method which is based on the relation between the $\pi M(t), \pi U(t), P(t)$ function at infinity asymptotic action [1].

3. Applications

GnRH secretion is enchanced in DIO mice

Because the baseline LH levels of the GnIRKO DIO mice were midway between those of control DIO and lean animals , and the stimulated levels were not different , We reasoned that differences in GnRH secretion could explain the differences in baseline LH levels. Ex vivo culture of the hypothalamus of mice (2, 4 & 18) was used to evaluate GnRH secretion patterns in animals of various genotypes and food circumstances, as well as GnRH release from the RIA-determined hypothalamic. GnRH gene expression is higher in control DIO mice than in GnIRKO DIO mice, which is consistent with control DIO mice's hypersecretion of GnRH.

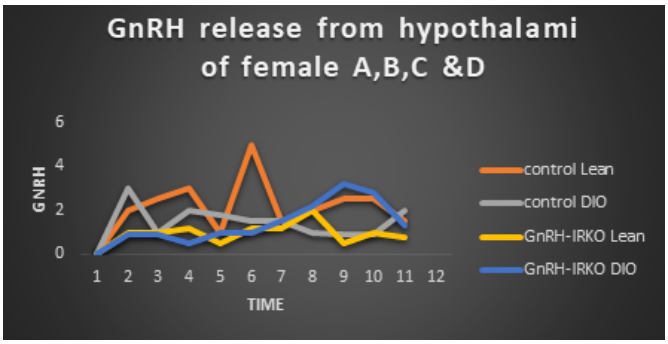
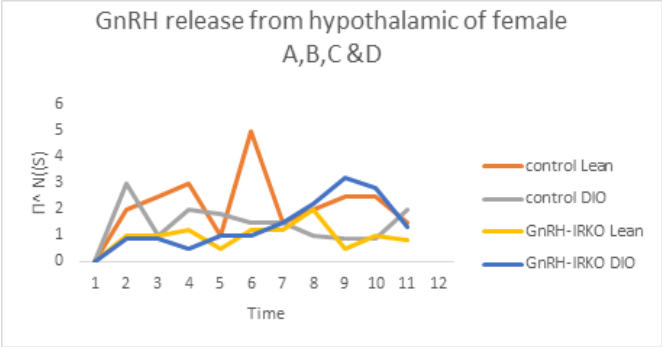


FIGURE 1. GnRH secretion is amplified in control DIO state

Hypothalamic from mice were excised, incubated in ex vivo culture,and GnRH determined by RIA. Graphical representation of GnRH release from hypothalamic of female (A) control Lean (B) control DIO, (C) GnIRKO lean and (D) GnIRKO DIO. The differences in GnRH secretion observed between lean, DIO control and DIO GnIRKO mice in the obese state imply that the GnRH neuron remains at least partially insulin sensitive in the hyperinsulinemic environment [16]. The pituitary and ovary also exhibit insulin sensitivity in DIO ; insulin-induced phosphorylation of Akt in these tissues is preserved in obese animals [17]. Given the homogeneity of the hypothalamus, we were unable to directly test in the insulin sensitivity of the isolated GnRH neuron in the obese animal.

4. Mathematical Results



5. Conclusion

We have established Some qualitative results for modelling degradation processes, generalized birth and death processes are added, which are special classes of semi markov processes [4]. The special emphasis is on the probabilities of the conditional state provided the cycles, which are most relevant for the processes of degradation.

The conclusion for the three instances of reliability decrease [4] was obtained from the figure. In summary , we provide evidence that the increased LH of obese female mice is partially due to insulin signalling at the GnRH neuron causing inceased GnRH secretion. Finally, we conclude that medical report and mathematical report are well fitted.

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Conflict of Interests

The authors declare that there is no conflict of interests.

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