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A Monte Carlo Method Used for the Identification of the Muscle Spindle

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Summary. In this chapter we describe the behavior of the muscle spindle by using a logistic regression model. The system receives input from a motoneuron and fires through the Ia sensory axon that transfers the information to the spinal cord and from there to the brain. Three functions which are of special interest are included in the model: the threshold, the recovery and the summation functions. The most favorable method of estimating the parameters of the muscle spindle is the maximum likelihood approach. However, there are cases when this approach fails to converge because some of the model's parameters are considered to be perfect predictors. In this case, the exact likelihood can be used, which succeeds in finding the estimates and the exact confidence intervals for the unknown parameters. This method has a main drawback: it is computationally very demanding, especially with large data sets. A good alternative in this case is a specific application of the Monte Carlo technique.

Key words: Exact logistic regression, likelihood function, Monte Carlo technique, muscle spindle.

21.1 The Biological System

The system we examine is a complex biological system called the muscle spindle, which is part of the skeletal muscles and is responsible for the initiation of movement and the maintenance of muscle posture. The effects of the imposed stimuli on the muscle spindle's fibers are transmitted to the spinal cord by the axons of sensory nerves closely associated with the muscle spindle. The discharge of the sensory axons is also modified by action potentials carried by the axons of a group of cells called motoneurons. The action potential is a localized voltage change that occurs across the membrane surrounding the nerve cell and axon, with amplitude approximately 100 mV and duration 1 ms. In this chapter we are interested in the discharge that occurs in the presence of an alpha motoneuron.

Let Y_t describe the firing process of the system. By choosing the sampling interval h, the observations of the output can be written as follows:

$$y_t = \begin{cases} 1, & \text{when a spike occurs in } (t, t+h] \\ 0, & \text{otherwise,} \end{cases}$$

where $t = h, \ldots, Nh$ and $T = Nh$ is the time interval in which the process is observed. We usually choose $h = 1$ ms. The input X_t imposed by the alpha motoneuron on the system consists of the observations x_t defined similarly.

21.2 System Modeling

In this section we present the logistic regression model that can be used for the identification of the system under the influence of an alpha motoneuron. This model extends the work of [2] and [3] used for the identification of neuronal firing systems. The firing of the system we study occurs when the potential of the membrane that surrounds the sensory axon exceeds a critical level called the threshold. The membrane's potential at the trigger zone is influenced both by internal and external processes.

The internal processes are responsible for the spontaneous firing of the system. This is an ability of the system to produce a series of nerve pulses on its own, by increasing the resting potential to the level of the threshold. Let ϕ_t denote the threshold potential level at the trigger zone at time t by $\phi_t = \theta_0 + \epsilon_t$, where ϵ_t is the unknown noise process that includes contributions of unmeasured terms that influence the firing of the system and θ_0 represents an unknown constant threshold. Other forms of threshold can also be considered that allow the threshold to vary with time [7]. Let V_t represent the recovery function which is described by a polynomial function of order k given by

$$V_t = \sum_{i=1}^{k} \theta_i \gamma_t^i,$$

where γ_t is the time elapsed since the system last fired and θ_i are the unknown coefficients.

External processes are responsible for the firing of the system when it is affected by external parameters such as the presence of a motoneuron. The function representing the effect of an alpha motoneuron on the muscle spindle at any given time t is based on a summation described by a set of coefficients $\{a_u\}$. The summation function is defined by

$$SF_t = \sum_{u \le t} a_u x_{t-u},$$

where x_{t-u} is the observation of the input at time $t - u$.

The logistic regression model that describes the effect of the covariates incorporated in the recovery and the summation function at any given time t is expressed as

$$\log\left(\frac{\pi_t}{1-\pi_t}\right) = \sum_{u \le t} a_u x_{t-u} + \sum_{i=1}^{k} \theta_i \gamma_t^i - \theta_0, \tag{21.1}$$

where π_t denotes the probability of an output spike to occur. The unknown parameters that have to be estimated are the coefficients $\{a_u\}$, the recovery function parameters θ_i and the constant threshold θ_0. More details about the logistic model given by (21.1) and the covariates included are given in [6].

21.3 Methods

21.3.1 The Maximum Likelihood Approach

The likelihood function is defined as the joint probability of the random variables whose realizations constitute the sample. For a sample of size n with observations $(y_1, \ldots, y_n)$, the corresponding random variables are $(Y_1, \ldots, Y_n)$. The probability density function of Y_t describes the contribution to the likelihood function of every single observation and is given by $P\{Y_t = y_t\} = \pi_t^{y_t}(1-\pi_t)^{1-y_t}$, $y_t = 0, 1$. Since the observations are assumed to be independent, the likelihood function is the joint probability

$$L_0 = P(Y_1 = y_1, Y_2 = y_2, \ldots, Y_n = y_n) = \prod_{t=1}^{n} \pi_t^{y_t}(1-\pi_t)^{1-y_t}, \tag{21.2}$$

where $\pi_t = \pi(x_{1t}, x_{2t}, \ldots, x_{pt})$ is the conditional probability that Y_t equals 1, given x_t, where p is the number of covariates included in the model. It is however more convenient to use the log of the likelihood function and therefore we have

$$l(y_t, \pi_t) = \log L_0 = \sum_{t=1}^{n} \left[y_t \log\left(\frac{\pi_t}{1-\pi_t}\right) + \log(1-\pi_t) \right]. \tag{21.3}$$

The probability π_t is related with the unknown parameters of the model through (21.1) and thus the likelihood function is considered as a function of the unknown parameters.

21.3.2 Drawbacks of the Maximum Likelihood Approach

The maximum likelihood approach is the most favorable method of estimation, but unfortunately it can fail completely or produce poor results in terms of the unknown parameters and their standard errors. These problems are caused by certain structures in the data, which occur when we deal with data sets that are small, or data sets that are large, but sparse. The most common numerical problem occurs when a collection of covariates separates the outcome, so that there is no overlap in the distribution of the covariates between the two possible outcome values. This phenomenon is called complete or quasi-complete separation and in these cases the maximum likelihood estimators do not exist as was demonstrated in [1] and [11]. The separation can be identified by the existence of one or more empty cells in the corresponding contingency tables. (An example of quasi-complete separation is described in Table 21.2. The empty cell where $X_{t-13} = 1$ and $Y = 1$ indicates quasi-complete separation.)

21.3.3 The Exact Logistic Regression

An alternative solution is to obtain the exact estimates of the unknown parameters. The idea of exact logistic regression (ELR) is to estimate some of the parameters of the model by replacing the remaining parameters in the likelihood function by their sufficient statistics. The likelihood function given by (21.2) can be written in the following form:

$$P(Y_1 = y_1, Y_2 = y_2, \ldots, Y_n = y_n) = \frac{\exp(\sum_{s=0}^{p} \beta_s w_s)}{\prod_{t=1}^{n}(1 + \exp(x_t \beta))}, \tag{21.4}$$

where $w_s = \sum_{t=1}^{n} x_{ts} y_t$ are the sufficient statistics, β is a vector of the unknown parameters and $\beta^T = (\beta_0, \beta_1, \ldots, \beta_p)$. In our case the vector β includes the coefficients $\{a_u\}, \theta_i$ $(i = 1, 2, \ldots, k)$ and θ_0. Suppose that we are interested in one of the regression parameters, regarding the remainder as a nuisance. Without loss of generality, we choose the parameter of interest to be β_p. It can be proved (see [8]) that the conditional likelihood is given by

$$f(w_p|\beta_p) = \frac{c(w_0, w_1, \ldots, w_p)\exp(\beta_p w_p)}{\sum_u c(w_0, w_1, \ldots, w_{p-1}, u)\exp(\beta_p u)}, \tag{21.5}$$

where the summation in the denominator is over all the values of u for which $c(w_0, w_1, \ldots, w_{p-1}, u) \geq 1$. The initial theory about ELR proposed by Cox in 1970 (see [4]) was considered computationally infeasible for many years and, despite the availability of fast numerical algorithms developed later (see [5] and [12]), there are cases where the data set is too large and the exact estimates cannot be obtained easily. This case corresponds to our example presented later, where we shall see that the requirements in computing time and memory are restrictive, because the data set is too large (15870 observations). A good alternative in this case is to obtain estimates of the exact results by using Monte Carlo techniques.

21.3.4 The Monte Carlo Approach

When it is not possible to store the exact permutational distribution, we could obtain Monte Carlo samples from this distribution. One naive approach would be to follow conventional Monte Carlo methods that lead to massive rejection of the samples that do not satisfy the constraints of the conditional distribution. This approach is easy to implement and does not require computer memory. However, it becomes inefficient very quickly even for relatively small samples. In this case one can use a network-based direct Monte Carlo sampling approach discussed in [10] which stores a network of vectors that satisfy the constraints of the conditional distribution given by (21.5). The samples are then drawn from this network and therefore this method is more efficient than the conventional Monte Carlo sampling. There is however a disadvantage as far as the memory is required for the construction and the storage of the network. The memory required depends on the specifics of the problem such as the sample size, the number of covariates in the model, the number of covariate groups and the proportion of responses. This technique is available on LogXact (see [9]).

Table 21.1. Table of the results.

	Estimates			95% Confidence Interval	
	Asymptotic(s.e.)	Exact	Monte Carlo	Exact	Monte Carlo
θ_0	−3.4186 (0.1317)	−3.4493	−3.4475	(−3.9435, −2.9905)	(−3.9551, −2.9655)
θ_1	0.0967 (0.0105)	0.0986	0.1002	(0.0629, 0.1351)	(0.0632, 0.1364)
a_1	0.2168 (0.2447)	0.2134	0.2142	(−0.7897, 1.0618)	(−0.7827, 1.1123)
a_7	1.7565 (0.1722)	1.7414	1.7534	(1.0975, 2.3617)	(1.1006, 2.4187)
a_{13}	−7.7503 (6.6326)	−2.2142	−2.2736	(−∞ , −0.4818)	(−∞ , −0.4877)
a_{19}	−7.8191 (6.7208)	−2.2480	−2.4730	(−∞ , −0.5272)	(−∞ , −0.4757)
a_{25}	−8.1085 (6.6810)	−2.5503	−2.3280	(−∞ , −0.8199)	(−∞ , −0.6439)
a_{31}	−8.1542 (6.7425)	−2.5838	−2.5827	(−∞ , −0.8594)	(−∞ , −0.8981)
a_{37}	−8.2998 (6.6745)	−2.7224	−2.7851	(−∞ , −0.9879)	(−∞ , −0.7965)
a_{43}	−2.7278 (0.7167)	−2.4404	−2.4465	(−∞ , −0.6608)	(−∞ , −0.6909)
a_{49}	−0.3193 (0.2464)	−0.3413	−0.3395	(−1.3670, 0.5291)	(−1.3919, 0.5245)

21.4 Results

In this section we provide a neurophysiological example which causes a breakdown in the maximum likelihood estimation. The data set includes two time series which consist of 259 input and 356 output spikes, recorded in a time interval of 15870 ms. The input is imposed to the muscle spindle by an alpha motoneuron and the output contains the discharge of the muscle spindle's sensory axon.

The attempt to fit the logistic regression model given by (21.1) using the maximum likelihood approach results in misleading conclusions, which are shown in Table 21.1. It is obvious that the estimates and the standard errors of the coefficients $a_{13}, a_{19}, a_{25}, a_{31}$, and a_{37} are very large compared with the other estimates, denoting a *problematic area* on the summation function. This occurs because of the quasi-complete separation, as illustrated in Table 21.2. This situation causes problems to the maximum likelihood estimation, which considers that the covariate X_{t-13} is a perfect predictor. The same situation applies for all the covariates of the *problematic area* and it causes the maximum likelihood method to diverge. A solution in this case is to perform exact estimation. The exact results and the confidence intervals are also shown in Table 21.1. The lower confidence bound for the estimates of the problematic

Table 21.2. 2×2 contingency table between Y and X_{t-13}.

	$Y = 0$	$Y = 1$
$X_{t-13} = 0$	4677	356
$X_{t-13} = 1$	257	0

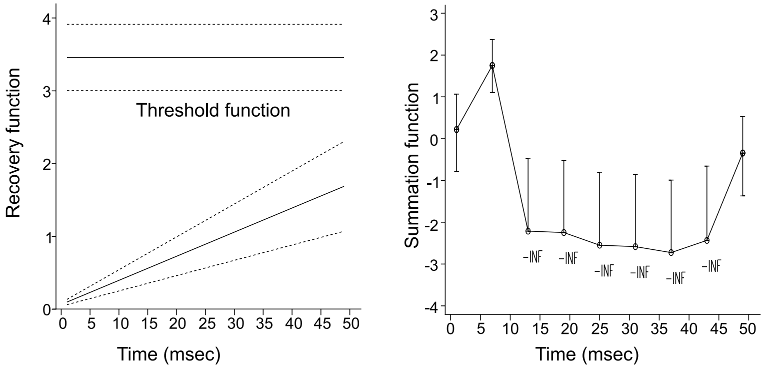

Fig. 21.1. (a) Monte Carlo estimates of the threshold and the recovery function. The dotted lines correspond to 95% confidence intervals. The recovery function does not cross the threshold, but the increase may be indicative of possible spontaneous firing. (b) Monte Carlo estimates of the summation function. The vertical bars represent the 95% confidence intervals of the a_u coefficients. The summation function accelerates for a very short period during the first 10 ms, and afterwards decelerates. This inhibitory behavior blocks the response of the system for about 40 ms.

area is $-\infty$, indicating that the data set contains observations at the extreme points of the sample space for these coefficients. An alternative solution is to perform Monte Carlo estimation by sampling 10,000 times from the appropriate conditional distribution. The estimates and their confidence intervals obtained by performing Monte Carlo estimation are shown in Table 21.1 and a graphical presentation is given in Fig. 21.1. All computations were performed on a Pentium, 1000 MHz PC. For consistency all the results are displayed to four decimal digits. The maximum likelihood estimates are compared with those of the ELR and the Monte Carlo respectively. The Monte Carlo estimation required 1/4 of the exact estimation computing time and 1/10 of the exact estimation memory requirements.

21.5 Discussion

In this chapter we have used a logistic regression model in order to describe the behavior of the muscle spindle when it is affected by an alpha motoneuron. The estimated coefficients of the summation function are positive for a very short period in the beginning, indicating an acceleration of the system's firing. However in the interval between 11–50 ms the system is blocked by the presence of the alpha motoneuron and its behavior is inhibitory. This becomes obvious from the negative values of the estimated coefficients. The recovery function is modelled by a first-order polynomial. The graphical presentation of the recovery function shows an increase, which tends to cross the threshold level. This fact indicates a tendency for possible activity of the system.

References

1. Albert, A., Anderson, J.A.: On the existence of maximum likelihood estimates in logistic models. Biometrika, **71**, 1–10 (1984).
2. Brillinger, D.R.: Maximum likelihood analysis of spike trains of interactive nerve cells. Biological Cybernetics, **59**, 189–200 (1988).
3. Brillinger, D.R.: Nerve cell spike train data analysis: a progression of technique. J. Am. Stat. Assoc., **87**, 260–271 (1992).
4. Cox, D.R.: *Modelling Binary Data*. Chapman & Hall, New York (1970).
5. Hirji, K.F., Mehta, C.R., Patel, N.R.: Computing distributions for exact logistic regression. J. Am. Stat. Assoc., **82**, 1110–1117 (1987).
6. Kotti, V.K., Rigas, A.G.: Identification of a complex neurophysiological system using the maximum likelihood approach. J. Biol. Syst., **11**, 189–204 (2003).
7. Kotti, V.K., Rigas, A.G.: A nonlinear stochastic model used for the identification of a biological system, In: Capasso, V. (ed.) *Mathematical Modeling & Computing in Biology and Medicine*. The Miriam Project Series, Progetto Leonardo, Escapulario. Co., Bologna, Italy (2003).
8. Kotti, V.K., Rigas, A.G.: Logistic regression methods and their implementation. In: Edler, L., Kitsos C.P. (eds.) *Recent Advances in Quantitative Methods for Cancer and Human Risk Assessment*. Wiley, New York (2005).
9. LogXact-5 for Windows, *User Manual*, Cytel Software (2002).
10. Mehta, C.R., Patel, N.R., Senchaudhuri, P.: Efficient Monte Carlo methods for conditional logistic regression, J. Am. Stat. Assoc., **95**, 99–108 (2000).
11. Santner, T.J., Duffy, D.E.: A note on A. Albert's and J.A. Anderson's conditions for the existence of maximum likelihood estimates in logistic regression models. Biometrika, **73**, 755–758 (1986).
12. Trichler, D.: An algorithm for exact logistic regression. J. Am. Stat. Assoc., **79**, 709–711 (1984).