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## **Dynamical analysis of erythrocytes under the assumption of cross-spectral coherence between blood cell counts and the *Dst* index**

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### **RESUMEN**

La posible influencia de la actividad solar sobre la salud humana a través de procesos biogeomagnéticos es en la actualidad un tema de gran discusión. Algunos procesos que ocurren en el Sol pueden afectar el entorno terrestre y producir grandes perturbaciones en el campo geomagnético. El índice *Dst*, el cual mide un promedio de las perturbaciones del campo geomagnético en el ecuador terrestre, es un buen indicador global de estas fluctuaciones. Por otro lado, los eritrocitos, los leucocitos y las plaquetas desempeñan un rol esencial en los sistemas vivos, ya que son responsables del transporte de oxígeno, de la respuesta del sistema inmunológico y de la coagulación, respectivamente. En este trabajo se analiza la posible asociación entre el número de células sanguíneas (colectadas de dos ovejas durante 1024 días consecutivos) y el índice *Dst*. Se ha encontrado que la correlación cruzada entre ambas series temporales es muy baja. Sin embargo, se encuentra una correlación significativa en las amplitudes del espacio de frecuencias. La identificación y análisis de los principales picos presentes en los espectros muestra que en ambas series se encuentra presente una importante componente en 7 días.

**PALABRAS CLAVE:** Biogeomagnetismo, índice *Dst*, eritrocitos, células sanguíneas.

### **ABSTRACT**

The possible influence of solar activity on human health through magneto-biological mechanisms is a prominent and controversial matter. Several physical mechanisms that occur in the Sun can affect the interplanetary environment of the Earth, and produce perturbations in the geomagnetic field. The *Dst* index, which measures the average disturbance magnetic field at the Earth's equator, is a good indicator of these global magnetic fluctuations. Erythrocytes, platelets and leukocytes play a key role in living systems because they are responsible for the transport of oxygen, coagulation and the immune response respectively. In the healthy subject, blood cell counts fluctuate and it is customary to talk of normal ranges or maximal limits. However, it has recently been reported that these fluctuations are scale-invariant. Daily fluctuations in the number of a given type of blood cell are expected to reflect the intrinsic dynamics of the hematologic system and its response to various intrinsic and extrinsic perturbations. We analyze blood cell counts from two sheep over 1024 consecutive days, and the *Dst* index. We found a low correlation between these temporal series, but we do find a significant correlation in frequency space. A significant peak around seven days is found in both series.

**KEY WORDS:** Bio-geomagnetism, *Dst* index, erythrocytes, blood cells, space weather.

### **INTRODUCTION**

Several earlier studies have analyzed the possibility of an association between life and geophysical activity, including the relationship between human pathologies and space weather features, such as solar wind or geomagnetic properties (see Mendoza and Díaz-Sandoval, 2000, and references therein). The association of myocardial infarctions or brain strokes with decreased cosmic ray flux and intense magnetic storms has been statistically studied by several authors (Hallberg *et al.*, 1991; Dorman *et al.*, 1993; Breus *et al.*, 1994; and Villoresi *et al.*, 1994).

Erythrocytes, leukocytes, and platelets play a key role in living systems (transport of oxygen, immune response, and coagulation, respectively). The influence (direct or indirect) of high frequency electromagnetic fields on erythrocytes has been analyzed (Kononenko and Ilyna, 1999), and the influence of strong static magnetic fields on the orientation of erythrocytes have been experimentally shown (Higashi *et al.*, 1993). However, studies on the possible influence (direct or indirect) of the geomagnetic field on different blood cells seen to be unavailable. This work attempts to determine if an association exists between geomagnetism, which is controlled by solar activity, and erythrocytes counts.

The *Dst* index reflects the global perturbations (known as magnetic storms) that the geomagnetic field can suffer as consequence of the excitation of the ring current system, located between 2 and 6 terrestrial radii. From the *Dst* index it is possible to determine when a magnetic storm takes place and also how intense is it.

The first section describes the analyzed blood cell data. The results of the data analysis are given in second section. A dynamic model for the evolution of erythrocytes is presented in the third section; two possible influences of *Dst* on red cells are modeled and the theoretical results are presented. Finally our conclusions are given.

### THE BLOOD CELLS

We consider time series corresponding to cell counts of blood from two sheep (Perazzo et al., 2000). Three different kinds of blood cells have been counted in each sheep:

erythrocytes (red blood cells), leukocytes (white blood cells), and platelets. The data series were collected over 1024 consecutive days and the range of time recorded was from November 28, 1996 up to August 24, 1999.

The data was collected from two castrated male sheep (one year old at the beginning of data collection) at Buenos Aires (~35S ~60W). Both sheep were diagnosed as healthy during the whole period by our in-house veterinarians. They were housed in individual pens. A few milliliters of blood were extracted every morning from the jugular vein, and the measurement of cell numbers was performed manually. The error of the measurements was  $10^4$  (i.e., ~1‰ respect to its mean value),  $10^3$  (~2‰), and  $10^3$  (~3‰) cells per  $\text{ml}^3$ , respectively for erythrocytes, leukocytes, and platelets. The measured values are consistent with normal ranges reported in literature for these animals (Jain, 1993).

Figure 1 shows the time series for blood cells. The upper, middle, and lower panels show the count for erythro-

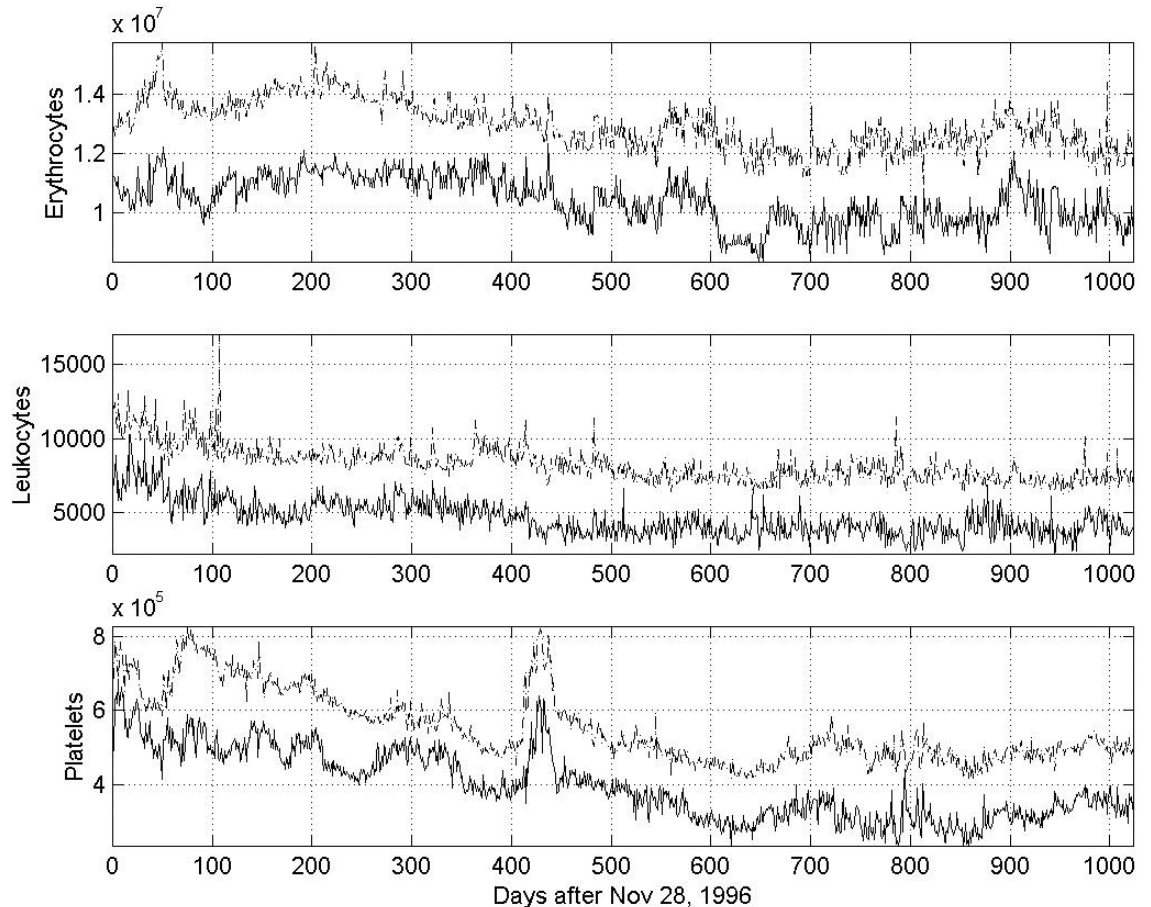


Fig. 1. Daily blood cell counts recorded over 1024 consecutive days from two healthy sheep. Upper panel: erythrocytes per  $\text{mm}^3$ . Middle panel: leukocytes per  $\text{mm}^3$ . Lower panel: platelets per  $\text{mm}^3$ . In order to clarify, the three series for one of the sheep (dashed lines) were shifted upward by 15% (erythrocytes), 100% (leukocytes) y 50% (platelets), with respect to their mean values.

cytes, leukocytes, and platelets, respectively. Each of two lines corresponds to one sheep. In order to permit a better view, the curve corresponding to one of the sheep was shifted upward in three panels: by 15% for erythrocytes, by 100% for leukocytes, and by 50% for platelets, with respect to their mean values (see Figure 1).

### HELIO-GEOMAGNETIC CONDITIONS AND BIOLOGICAL RHYTHMS

In spite of the major importance of the knowledge of the influence level of helio-geomagnetic conditions on living systems, very few works have been published on this issue. However Breus *et al.* (1995) suggested the possibility that this kind of influence can be responsible for several rhythms in biological systems on Earth. In order to find possible associations between the typical rhythms of blood cells counts and *Dst*, a spectral analysis of both series is presented here.

As a first step to find a possible connection between the helio-geophysical (known also as space weather) conditions, the cross correlation between the *Dst* and each blood cells series is computed. This correlation presents very low values, even when a delay of blood series is considered respect to the daily values of the *Dst* index (in order to simulate a possible late effect of the geomagnetic field). We use the *Dst* series with a time resolution of one hour, which was obtained from the NOAA NGDC Solar Terrestrial Physics Division datasets (Website: [ftp://ftp.ngdc.noaa.gov/STP/GEOMAGNETIC\\_DATA/INDICES/DST/](ftp://ftp.ngdc.noaa.gov/STP/GEOMAGNETIC_DATA/INDICES/DST/)). The daily *Dst* values were obtained from an average of this hourly values.

Figure 2 shows the *Dst* time series, a widely-used signal to determine global space weather conditions, correspond-

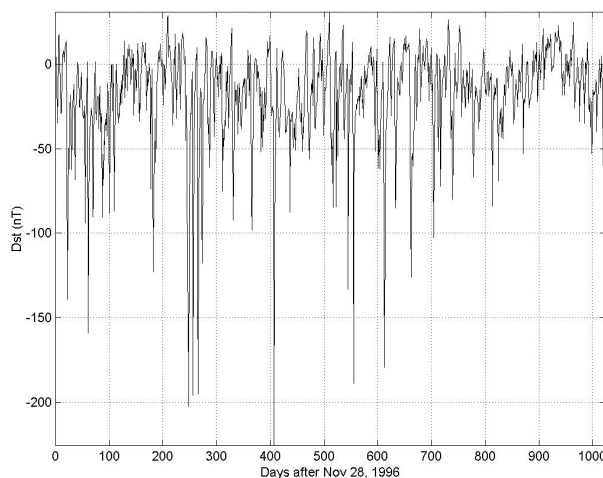


Fig. 2. Time series for the *Dst* index.

ing to the same period of time over which the blood data were collected. In this figure it can be observed that this period was magnetically very active, with plenty of moderate storms, and with more than 10 intense magnetic storms. Moderate and intense magnetic storms can be observed from *Dst* as follows: a moderate (intense) magnetic storm is present when the *Dst* index reaches negative values, lower than  $-50$  nT ( $-100$  nT) (Gonzalez *et al.*, 1994).

It is well known that the interplanetary medium presents typical periods associated with solar processes: 22 and 11 years periods attributable to the solar cycle (Cliver *et al.*, 1996; Mavromichalaki and Vassilaki, 1998), 26-28,  $\sim 13.5$  days to the solar rotation (Mursula and Zieger, 1996),  $\sim 7$  days (Breus *et al.*, 1995 and reference therein), and 24 hours to the Russell McPherron effect (Siscoe and Crooker, 1996).

The seven day period is present in a considerable quantity of interplanetary parameters of solar origin (*e.g.*, bulk velocity, density, and temperature of solar wind), as well as in other geomagnetic parameters besides *Dst* (Breus *et al.*, 1995 and references therein). It is known that these peaks originate from solar rotation combined with the existence of four magnetic sectors per gyration. These sectors are expanded in quarters of  $\sim 90^\circ$  each and the magnetic field, measured by a spacecraft, changes its sign (toward the Sun or toward the outer heliosphere) when the satellite crosses from one sector to the nearest neighbor. Thus, the interplanetary space near Earth presents features associated with the current sheet which separates two consecutive sectors, that is to say, four times per solar rotation of 27 days (Wilcox and Ness, 1965).

The power spectrum for every series (blood and *Dst*) is calculated, using the Maximum Entropy Method (MEM) and the Welch algorithm. While the direct cross-correlation is very low, a notable correlation ( $\sim 0.4$  -  $\sim 0.6$ ) in the Fourier space is found between the *Dst* series and the three kinds of blood cells. The correlation between *Dst* and erythrocytes is slightly greater than the rest. The lowest correlation is found for platelets.

The spectra of erythrocytes and *Dst* are compared in Figure 3. The upper panel (each curve corresponds to one sheep) displays the spectrum for red cells, and it shows significant peaks at  $\sim 7$ , 12, and 20 days. The lower panel displays a window of the power spectrum of *Dst*, where notable peaks at  $\sim 7$ , 9.5, 13.5, and 27 days, can be seen. Thus, both spectra show a significant activity at a period near to 7 days.

### A MODEL TO REPRESENT THE DYNAMIC OF ERYTHROCYTES: MACKAY-GLASS

In this section we attempt to identify mechanisms of space weather conditions which may influence the blood. In

particular, in order to investigate responses of the circulating erythrocyte number to geomagnetic conditions, we analyze slight variants of the Mackey Glass model (Mackey and Glass, 1977 and Mackey, 1997). This model, considered a paradigm of delayed non-linear dynamical systems, is very simple and represents the production of red cells (hematopoiesis), regulated by feed-back control systems. The injection of new mature erythrocytes at time  $t$  is determined from the number of circulating red cells at time  $t-\tau$ . If  $X(t)$  denotes the population of mature red cells, its dynamic is regulated by:

$$\frac{d}{dt}X(t) = F_0 \frac{\vartheta^n}{X^n(t-\tau) + \vartheta^n} - \gamma X(t) \quad (1)$$

with  $X(t) = f(t)$  for  $t \in (-\tau, 0)$ .

Here  $\gamma$  is the cell mortality rate,  $\theta$ ,  $n$  y  $F_0$  are constant parameters of the model, and  $f(t)$  represents the initial condition for  $X(t)$ . The first term of right hand side of (1) corresponds to the cellular production determined by the erythrocytes density at time  $t-\tau$ .  $\tau$  represents the delay between the production of precursor cells and the liberation of mature cells into the blood flux. The second term represents the death

of mature cells. The values for the constants  $F_0$ ,  $\theta$ ,  $\gamma$ ,  $n$ , and  $\tau$ , have been taken from experimental data of normal organisms, and their values are:  $F_0=7.62 \times 10^{10}$  cells/kgday,  $\theta = 2.47 \times 10^{11}$  cells/kg,  $\gamma = 2.31 \times 10^{-2}$ /day,  $n=7.6$  y  $\tau=6$  days (values taken from (Mackey, 1997)).

In order to study a possible influence of space weather-condition on the amount of circulating red blood cells, the response of the Mackey-Glass system to a low external driving force is analyzed. In particular the influence of a harmonic stimulus on the system is studied using two simple modifications to Equation (1):

(i) additive harmonic driven, *i.e.*,

$$\frac{d}{dt}X(t) = F_0 \frac{\vartheta^n}{X^n(t-\tau) + \vartheta^n} - \gamma X(t) + A \sin(\Omega t)$$

(ii) death rate ( $\gamma$ ) perturbed by a harmonic term, *i.e.*,  $\gamma = \gamma_0 + A \sin(\Omega t)$ .

In both cases the external frequency ( $\Omega$ ) corresponds to any of the main peaks of the *Dst* spectrum. Both models have been numerically solved with fourth-order Runge-Kutta integration techniques.

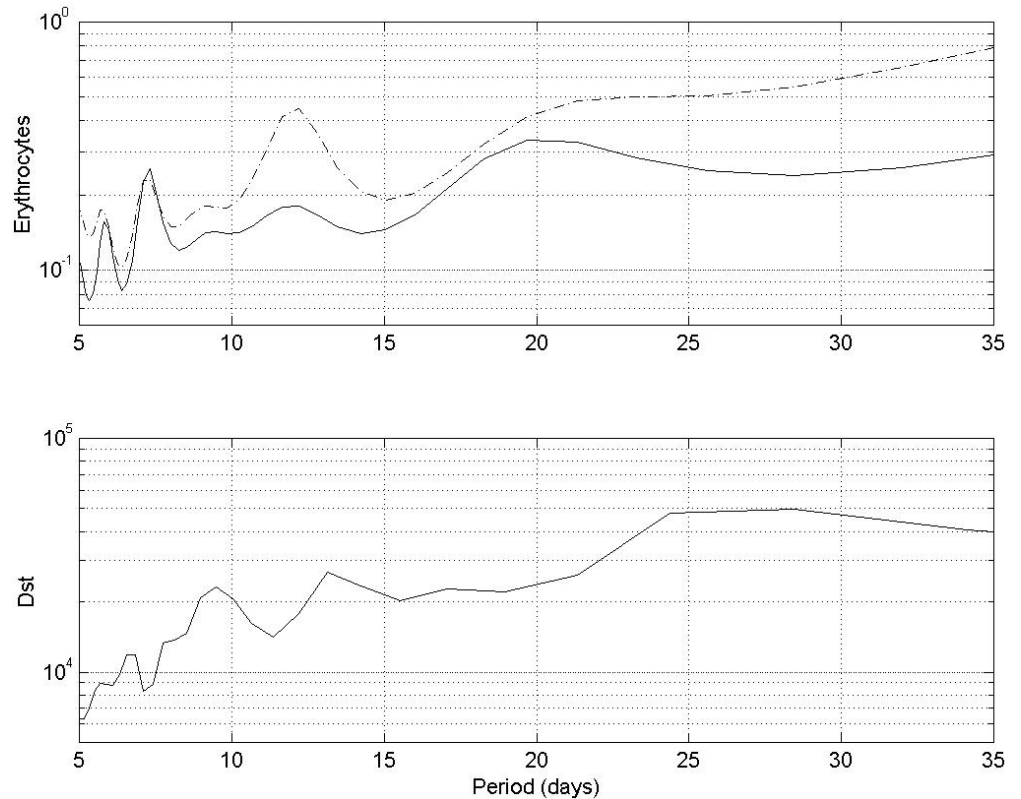


Fig. 3. Power spectra for erythrocytes (upper panel) and for the *Dst* index (lower panel). Each line in the upper panel corresponds to one sheep.



A bifurcation diagram for the modified, as in case (i), Mackey-Glass system is presented in Figure 4. The main panel of the figure shows the temporal evolution of  $E(t) = X(t) / X^*$  evaluated only for times (return map)  $t = t_0 + nT$ ,  $n \in \mathbb{N}$ , with  $t_0$  an arbitrary initial time, and  $T = 2\pi/\Omega = 13.5$  days a period that corresponds to one of the main peaks of the spectrum of  $Dst$ , as the amplitude of the external driven ( $a = A/X^*$ ) is changed. The intensity of the external driven is normalized by the number of cells for the stationary state ( $X^* = 3.3 \times 10^{11}$  cells/kg) of Equation (1). This kind of diagram shows qualitative changes to the structure of the systems' evolution, when some of the control parameters are continuously varied.

It is possible to observe a critical value for  $a$  ( $a \sim 0.1$ ), or bifurcation point, where the system realizes a transition from a periodic (with period  $T$ ) answer to another with period  $2T$ . For values of  $a$  lower than 0.1 the system presents a periodic answer of very low amplitude (the system damps the perturbation). However, for cases with  $a$  greater than 0.1 there is an important amplification. Similar qualitative results are obtained for other values of  $T$  and for cases as in (ii), in which a harmonically perturbed mortality rate is considered.

Several important peaks of  $Dst$  are not observed in the spectrum of erythrocytes, e.g.,  $T \sim 9.5, 13.5$  y 27 days (see Figure 3). On the other hand, (see Figure 4), the effect of a weak harmonic additive driven ( $a \ll 0.1$ ) on the Mackey-Glass system produces a damped response. When  $a \sim 0.01$ , that is to say a significant amplitude of approximately the source term over two, the population of red cells  $E(t)$  oscil-

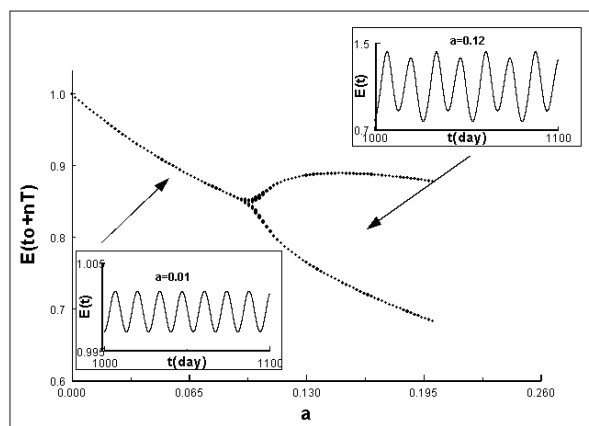


Fig. 4.  $E(t = nT + t_0)$  as a function of  $a$  (stroboscopic map).  $n$  is a whole number,  $T = 13.5$  days, and  $t_0$  a fixed reference time. Each internal figure shows a periodic solution of the system, with period  $T$  (left and lower panel) or  $2T$  (right and upper panel), corresponding to different values of  $a$ .  $a = A/E^*$ , is the dimensionless harmonic driven amplitude.  $E^* = 3.3 \times 10^{11}$  cells/kg is the number of cells for the stationary state.

lates with  $\sim 0.004$ , a very low amplitude. For lower values of  $a$ , the effect is even less. Thus, even under the hypothesis of the existence of this weak effect, it could not be manifested in the computed spectrum due to the resolution of blood data analyzed.

## CONCLUSIONS

The connection between the  $Dst$  time series and three blood cell series (erythrocytes, leukocytes, and platelets) of two sheep was analyzed.

Even with plenty of geomagnetic activity over the study period, including several intense magnetic storms, the temporal evolution of the blood cell series does not present an appreciable direct response (neither instantaneous nor delayed) to global geomagnetic activity. However, a perceptible spectral correlation between  $Dst$  and each of the three kinds of blood cells is present.

The result of our simulations indicates that the effect of: (i) a harmonic perturbation added to the source term in the Mackey-Glass system and (ii) a mortality rate of mature erythrocytes harmonically perturbed, are damped by the dynamical system. Thus, the Mackey-Glass system presents low susceptibility when harmonic forces are present. Therefore, under the hypothesis of a weak influence of  $Dst$  on  $X$  through this kind of coupling, the resolution ( $\sim 1\%$ ) of the analyzed blood series prevents appreciation of this effect. However, although most of the main peaks of  $Dst$  are not observed in the spectrum of blood cells, a peak ( $T \sim 7$  days) is observed in both spectra ( $Dst$  and erythrocytes).

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