identifying potentially meaningful interval-pattern 'bytes'. The physiological significance, i.e. the information carrying value, of interval-pattern bytes must be determined empirically by reference to some external event or parameter.

The apparent unpredictability of the entropy of specified symbol sets is a clear indication that certain of these sets have a special meaning for the system; such clusters of intervals may well be recognized in the system as a 'word' Of special note are the clusters $----$ and $++++$, because simple cases of this kind are readily subject to experimental verification.

The presence of large entropy values of certain symbol sets seems to document the widely held belief that there is much noise in a spike train. Nonetheless, there appears to be 'signal' in the presence of that noise, and our technique seems able to distinguish between the two in a highly specific way.

The main advantage of our relative entropy scheme is that it permits rational development of hypotheses. Out of the vast array of possibilities we are able to order symbol sets of different length and content in a rational way that permits systematic development of hypotheses for empirical testing. For example, we might postulate that symbol sets with the most relative entropy are less biologically meaningful than sets with the least entropy.

Average % maximum entropy for symbol groups. Consistent with the observations on average maximum entropy, the average % maximum entropy increases from digrams to quadgrams. However, when sign is taken into account (table 2), it is clear from the overall negative averages that many of the symbol sets in a group had substantially less entropy than the theoretical maximum. Note that the least indication of disorder (entropy) was in the quadgrams. While the large SDs preclude statistically significant differences among the groups, they do serve to emphasize the fact that there was a wide variation in the percentage of maximum entropy for individual symbol sets within a given group. It seems reasonable to suspect that the spike train is not random and independent, but in fact contains 'information'.

When the averages are tallied separately for those symbol sets that are below or above 0% (table 2), other significant facts become evident. For example, most of the symbol sets have markedly less entropy than the overall group average; note that the averages are about the same for digrams, trigrams and quadgrams and that the SDs in each case are distinctly smaller than those of symbol sets with positive entropy averages.

Thus, we believe that these results provide a basis for several rather profound conclusions about trains of nerve impulses: 1. that the train of intervals is not random and independent, 2. that the signal contains a mixture of noise and of 'information', and 3. that some groups of intervals seem to have a meaning for the system as a 'byte' of successive intervals.

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Effect of menstrual stress on serum lipid levels

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Summary. The effect of menstrual stress on serum lipid levels has been investigated in 28 healthy unmarried student nurses aged between 19 and 25 years, with histories of regular 26-30 day menstrual cycles. There were definite and similar patterns of changes in serum cholesterol, phospholipids and triglycerides during different phases of the menstrual cycle.

It is now well recognized that many women become distressed in response to their menstrual cycle. In most cases symptoms appear to peak within 3-4 days prior to the onset of menstrual flow and often disappear when the flow starts[3]. This has led to the coinage of the term premenstrual tension[4]. The term 'paramenstrum' includes 4 days prior to the onset of menstruation and 4 days of menstruation. The other days in the cycle comprise the intermenstrum[5]. Results of the serum lipid studies performed during the menstrual cycle vary and are somewhat contradictory[6-10]. Our earlier work on preoperative stress and serum cholesterol levels led us to undertake the present investigation so as to understand the correlation, if any, between menstrual stress and serum lipids[11].

Materials and methods. 28 unmarried healthy female student nurses aged 19-25 years with histories of regular 26-30 day menstrual cycles were selected as subjects for menstrual stress investigation. They did not take any medication or hormone preparation for 3 months before the study. For each subject the serum total cholesterol, phospholipids and triglycerides were estimated on 5 ocassions during the menstrual cycle, viz. 1. 8-9 days after mid-cycle (this time has been designated as end-cycle), 2. the day of menstruation (i.e. 1st or 2nd day), 3. the day after menstruation has ceased (usually 5th or 6th day after starting) when estrogen and progesterone concentrations are generally low, 4. at mid-cycle (assessed as 14 days before the predicted date of menstruation) when estrogen concentrations are normally at their highest, and 5. at end-cycle when the progesterone peak is expected. On all occasions fasting blood samples were collected in the morning between 8.30 and 9.00 a.m. Serum total cholesterol, phospholipids and triglycerides were estimated according to the methods of Zak[12], Connerty et al[13], and Carlson[14], respectively. Means and standard errors were calculated and results were tested for statistical significance by means of a paired t-test.

Results. The results recorded in the tables clearly indicate a definite and similar pattern of changes in serum levels of total cholesterol, phospholipids and triglycerides on different days of the menstrual cycle. Though the fluctuations in serum lipid fractions were of lower magnitude, they were statistically significant. The salient features of the observed fluctuations in levels of serum total cholesterol, phospholipids and triglycerides were: relatively low values at end-cycle (premenstrual tension), an increase on the 1st or 2nd

Table 1. Serum lipid profile during menstrual cycle

Observation	Cholesterol (mg%)	Phospholipids (mg%)	Triglycerides (mg%)
End-cycle	154.40±4.2	180.55±6.87	85.20±4.14
Beginning of menstruation	164.84±4.9	194.89±6.56	93.30±5.20
End of menstruation	152.80±4.0	183.05±6.57	85.73±5.65
Mid-cycle	165.00±3.7	201.17±6.76	91.63±4.77
End-cycle	153.10±4.0	183.18±7.14	84.70±3.97

Values are mean ± SEM.

Table 2. Statistical analysis

	Cholesterol			Phospholipids			Triglycerides		
Difference in the observations	Mean difference	t	p	Mean difference	t	p	Mean difference	t	p
8–9 days after mid-cycle versus beginning of menstruation	+10.44	6.65	<0.001	+14.34	2.80	<0.01	+9.10	3.01	<0.01
Beginning of menstruation versus end of menstruation	−12.04	3.07	<0.01	−11.84	1.56	>0.10 NS	−7.57	2.48	<0.05 Significant
End of menstruation versus mid-cycle	+12.20	3.51	<0.01	+18.12	2.65	<0.05 Significant	+5.90	1.66	>0.10 NS
Mid-cycle versus 8–9 days after mid-cycle	−11.90	3.87	<0.001	−17.99	5.45	<0.001	−6.93	3.60	<0.01

− = fall; + = rise; NS, not significant.

day of menstruation, a fall at the end of menstruation (i.e. 5th–6th day), and an increase at mid-cycle followed by a fall at the end of the cycle.

Discussion. The statistical analysis reveals that the observed fluctuations in serum lipid levels are significant except in 2 cases, viz. a) a fall in phospholipid level when results for the beginning of menstruation and end of menstruation are compared and b) a rise in triglyceride level when results for the end-of-menstruation day and for mid-cycle are compared. At this juncture it is difficult to offer any comment on the statistically insignificant fall in phospholipid level and rise of triglyceride levels. The observed low values for the serum lipid level on the end-of-menstruation day (i.e. 5th or 6th day) suggest its probable usefulness as an effective control value when females are to be used as experimental subjects. Whether directly or indirectly, estrogens are known to act upon the entire endocrine system. However, the pituitary, the adrenal gland and the thyroid are most susceptible to estrogenic secretions[16]. The serum lipid changes observed during the different days of the menstrual cycle are attributed to the fluctuating levels of sex steroid hormones and other hormones. Boyd et al.[6] reported the lowest serum cholesterol and phospholipid levels at the ovulation phase of the menstrual cycle. Adlercreutz and Talqvist[7], however, indicated that the lipid level was highest during ovulation. In the present investigation the lipid values are higher on the 1st day of menstruation, i.e. menstural stress, and also at mid-cycle, i.e. ovulatory stress, as compared with on the end-of-menstruation day. In addition Adlercreutz and coworkers[8] reported that the level of free cholesterol in the serum rises at the luteal phase while total cholesterol and phospholipids increase significantly from the beginning of the menstrual cycle until ovulation and decline throughout the luteal phase. Gustafson et al.[9] reported that the serum free and total cholesterol, total phospholipids and triglycerides are higher during the proliferative phase and that serum free cholesterol and lysolecithin varied inversely during different phases of the menstrual cycle. Reijo Punnonen[10] observed minimal changes in serum lipids during the menstrual cycle. Low-Beer et al.[16] have reported low values for serum cholesterol and triglycerides at the end of menstruation, a rise at mid-cycle and a fall 9 days after mid cycle. According to the definition of paramenstrum one would expect elevation of serum lipids during premenstrual tension, but in the present investigation we have observed a fall in serum lipids and the levels were comparable with those observed at the end of menstruation. Premenstrual tension refers to disturbances of mood and physical symptoms such as nausea, fuzzy vision etc. The menstrual cycle is also affected by factors like malnutrition, passion and a variety of psychosocial stress conditions[16]. Our subjects in the present investigation had neither emotional disturbances nor any difficulty in concentration in day-to-day work during the end-cycle and the other phases of the menstrual cycle. This may explain the observed low serum lipid levels at the end of the cycle in the subjects of the present series. It is felt that more frequent blood sampling would be necessary to throw more light on the precise timing and extent of the cyclical changes taking place throughout the phases of the menstrual cycle.

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