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Supplementary Information

Time Series Analysis

The generic element sample can be represented as:

$$y_t = \sum_{j=0}^{n} (\alpha_j \cos(w_j t) + \beta_j \sin(w_j t)) \quad (1)$$

Assuming that T = 2n is even, this sum comprises T functions whose frequencies

$$w_j = \frac{2\pi j}{T}, \text{ j=0...., n=} \frac{T}{2} \quad (2)$$

are at equally spaced points in the interval [0, π].

In the analysis of cyclical fluctuations in CMR_{glc}, there are as many nonzeros elements in the sum under (1) as there are data points, for the reason that two of the functions within the sum-namely $\sin(\omega_0 t) = \sin(0)$ and $\sin(\omega n t) = \sin(\pi t)$ -are identically zero. It therefore follows that, the mapping from the sample values to the coefficients constitutes a one-to-one invertible transformation. The similar situation arises in the slightly more complicated case where T is odd.

The angular velocity $\omega j = 2\pi j/T$ relates to a pair of trigonometrical components which accomplish j cycles in the T periods spanned by the data. The highest velocity $\omega n = \pi$ has been termed the Nyquist frequency. If a component with a higher frequency than π were included in the sum in (1), then its effect would be indistinguishable from that of a component t with a frequency in the range [0, π].

Applying a heuristic approach in the calculation of the Fourier coefficients, an ordinary regression procedure could be used to fit equation (1) to the data. In which case, there would be no regression residuals, since the total of T coefficients from T data points is being 'estimated'. In other words, a set of T linear equations in T unknowns could be solved. The cosine coefficients are regression coefficients that show the degree to which the respective cosine functions are correlated with the data at the respective frequencies. Similarly, the sine coefficients tell the degree to which the respective sine functions are correlated with the data at the respective frequencies. Multiple regression procedure is not appropriate in this case, since the vectors of 'explanatory' variables are mutually orthogonal. The T applications of a univariate regression procedure would be appropriate for this purpose.

The variance of the sample could be expressed as:

$$\frac{1}{T}\sum_{t=0}^{T-1}(y_t - \bar{y})^2 = \frac{1}{2}\sum_{j=1}^{n}(\alpha_j^2 + \beta_j^2)^2$$

$$\frac{2}{T^2}\sum_j \left\{ (\textstyle\sum_t y_t \cos\omega_j t)^2 + (\sum_t y_t \sin w_j t)^2 \right\} \quad (3)$$

The proportion of the variance which is attributable to the component at frequency ωj is $(\alpha^2 j + \beta^2 j)/2 = \rho^2 j/2$, where ρj is the amplitude of the component. The Fourier frequencies increase in number at the same rate as the sample size T. Given a finite variance of the sample, and if there are no regular harmonic components in the process generating the data, then the proportion of the variance attributed to the individual frequencies decline as the sample size increases. However, if there is a regular component within the process, then the proportion of the variance attributable to it converge to a finite value as the sample size increases. A graphic representation of the decomposition of the sample variance could be scaled to the elements of equation (3) by a factor of T.

The graph of the function $I(\omega j) = (T/2)(\alpha^2 j + \beta^2 j)$ is known as the periodogram. In other words, the periodogram values are computed as the sum of the squared sine and cosine coefficients at each frequency (time n/2). The periodogram values can be interpreted in terms of variance (sums of squares) of the data at the respective frequency or period. Period is calculated as the inverse of frequency. It is the number of observations that is necessary in order to complete one cycle at the respective frequency. To remove random fluctuations, it is customary to smooth the periodogram. The spectral density estimates are obtained by smoothing the periodogram values with a weighted moving average. There are several moving average smoothing windows [1-4]. The periodicities often only emerge when examining the spectral densities; that is, the frequencies, that contribute most to the overall periodic behavior of the series. The spectral density at a frequency f gives the rate of variance contributed by many adjacent frequencies to the variance of x per unit frequency. The spectral density peaks of a given function x provides useful information on the periodicity, magnitude, and localization of brain function.

Stationarity Assumption

To examine the stationarity assumption of the time series, we applied the Augmented Dickey-Fuller (ADF) test using the software package STATA (Stata Corp LLC, College Station, TX, USA). Unit roots can cause unpredictable results in the data of a time series analysis. The ADF test is the unit root test for stationarity [5]. The ADF is applied because it can handle more complex models that the Dickey-Fuller test, and it is more powerful. However, it has a relatively high Type I error rate (i.e incorrect rejection true null hypothesis). After inspection of the dataset we chose the appropriate regression model, with constant. The ADF adds lagged differences to these models. In general, the ADF test is similar to the Dickey-Fuller test, using the model:

$$Dy_t = \alpha + \beta_t + \gamma y_{t-1} + \delta_1 Dy_{t-1} + \ldots + \delta_p - {}_1 Dy_{t-p} + 1 + \varepsilon_t \quad (4)$$

Were α is a constant, β the coefficient on a time trend and p the lag order of the autoregressive process. Imposing the constraints α = 0 and β = 0 corresponds to modeling a random walk and using the constraint β = 0 corresponds to modeling a random walk with a drift. We chose a lag length so that the residuals were not correlated. By including the lags of the order p the ADF formulation allows for higher-order autoregressive processes. This means that the lag length p has to be determined when applying the test. We used the t-statistic associated with the Ordinary least squares estimate of γ .The level of significance was set at 0.05. The null hypothesis of the Augmented Dickey-Fuller t-test is:
H_0: γ = 0 (i.e., the data needs to be differenced to make it stationary);
H_1: γ < 0 (i.e., the data is stationary and does not need to be differenced).

The Dickey-Fuller t-test statistic (DF_T) was compared with the tabulated critical value [5]. If the DF_T statistic is more negative than the table value, reject the null hypothesis of a unit root. The DF_T statistic suggest that the time series data were strongly stationary without transformation.

$$DF_T = \frac{\hat{}\gamma}{SE(\hat{}\gamma)} \quad (2)$$

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