Complexity v1.0 Documents

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Complexity is a toolkit used to analyze the complexity of resting state fMRI (rs-fMRI) data. In order to run Complexity, the toolbox of "Tools for NIfTI and ANALYZE image" is needed which can be downloaded from Matlab Central,
http://www.mathworks.com/matlabcentral/fileexchange/8797-tools-for-nifti-and-analyze-image.
The current version includes a pre-processing module and four different methods or modules to calculate the entropy of rs-fMRI:

1. ApEn (Approximate Entropy)
ApEn was proposed by Pincus 1991 (1), which has been widely applied to biological signals such as EEG, EKG and hormonal release. We are the first group to introduce ApEn for the analysis of the complexity of rs-fMRI (2).

ApEn measures the logarithmic likelihood (or conditional probability) that runs of patterns that are close (within the same tolerance width r) for m contiguous observations remain close on subsequent incremental comparisons ($m+1$). The steps involved in calculating ApEn are as follows:

1. For a time-series u(t) with N data points, form sequence of vectors x(1), x(2),...,x(N) by x(i) = [u(i),...,u(i+m-1)].
2. For each i, $1 \leq i \leq N-m+1$, construct $C_i^m(r)$ ={number of x(j) such that d[x(i),x(j)] ≤ r }/ (N+m-1), where d[x(i),x(j)] = max|u(i+k-1)-u(j+k-1)| for k = 1,2,...,m, given by the maximum of the difference of the scalar components of x(i) and x(j), represents the distance between the vectors.
3. Calculate $C_m(r) = \dfrac{\sum_{j=1}^{N-m+1} C_i^m(r)^j}{N-m+1}$.
4. Repeat steps 1, 2 and 3 for $m+1$ contiguous observations to obtain $C_{m+1}(r)$.
5. ApEn is defined as: ApEn(m, r, N) = ln $C_m(r)$ - ln $C_{m+1}(r)$.

2. Cross-ApEn (Cross Approximate Entropy)
The calculation of C-ApEn is identical to that of ApEn except two different time series are compared. Different from the ApEn algorithm above, the distance is defined:
$$d[x_m(i), y_m(j)] = max\{u(i+k) - v(j+k), 0 \leq k \leq m-1\}$$

3. SampEn (Sample Entropy)
Sample entropy was proposed to minimize the bias of ApEn due to the inclusion of self-matching (3). SampEn is similar to ApEn except that SampEn does not include self-matching patterns.
$$sampEn = -ln\frac{A}{B}$$
A is the number of matching pairs with d[x(i), x(j)] < r of length m+1. B is the number of matching pairs with d[x(i), x(j)] < r of length m.

4. MSE (Multiscale Sample Entropy)
MSE was developed to differentiate random noise from complex signals exhibiting self-similarity across multiple time scales (4). Sample entropy can be regarded as a special case of MSE at the

original time scale of s = 1, where s is skipping parameter. The time series are constructed by averaging the data point with length of a. The modified series are: y(1), y(2), ..., y(N/a),

$$y_j^a = 1/a \sum_{i=(j-1)a+1}^{ja} u_i$$

Then the MSE can be calculated by SampEn.

5. Wavelet-MSE
This module is under development.

How to Use

Before the calculation, you can use the pre-processing module which includes low pass filtering and linear detrending. We highly recommend the use of detrending since drifts will affect the count of matching patterns and the calculation of entropy.

1. Input
Step 1: Select Input Directory
Input "3d" or "3D" for 3D series, otherwise the series will be considered as 4D series.
Then click "Open".
It will take some time to input the data. But if the progress bar does not move and there is an error in the commend line, make sure that you have downloaded the "Tools for NIfTI and ANALYZE image" toolbox by Jimmy Shen and add the folder directory to the Matlab PATH.

Step 2: Select Brain Mask
Generate a brain mask file using the BET program and select the mask file. The mask dimension and the image dimension should be the same, or the software will display an error and cannot work.

Step 3: Verify Orientation
The mask generated might be not in the right orientation. In this step, you can modify the orientation to match that of the images.

Step 4: Set the Parameters
m must be a positive integer, which represents the window length.
r is the percentage of standard deviation of the series data, so it must be a positive number ranging from 0 to 1.
r and *m* can take multiple values. Enter the values separated by comma, like r = 0.2, 0.3.
For MSE, there is another parameter, scale. It must be a positive integer.

Step 5: Set the seed voxel for C-ApEn
For C-ApEn, the user can manually select the seed voxel(s) using GUI.

2. Output
Step 6: Select Output Directory
Select the directory for the output file.

Step 7: Calculation
If you have set the images data, mask, parameters, and output folder, this step will calculate ApEn, dampen, cross ApEn or MSE.

Step 8: Display
Display the output file.

Reference

1. Pincus SM. Approximate entropy as a measure of system complexity. Proceedings of the National Academy of Sciences of the United States of America 1991;88(6):2297-2301.
2. Liu CY, Krishnan AP, Yan L, Smith RX, Kilroy E, Alger JR, Ringman JM, Wang DJ Complexity and Synchronicity of Resting State BOLD FMRI in Normal Aging and Cognitive Decline *J Magn Reson Imaging*. 2013;38(1):36-45
3. Richman JS, Moorman JR. Physiological time-series analysis using approximate entropy and sample entropy. Am J Physiol 2000;278:H2039–H2049.
4. Costa M, Goldberger AL, Peng CK. Multiscale entropy analysis of biological signals. Phys Rev E Stat Nonlin Soft Matter Phys. 2005 Feb;71(2 Pt 1):021906. Epub 2005 Feb 18.