Review

Small-world network properties in prefrontal cortex correlate with predictors of psychopathology risk in young children: A NIRS study

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ABSTRACT

Near infrared spectroscopy (NIRS) is an emerging imaging technique that is relatively inexpensive, portable, and particularly well suited for collecting data in ecological settings. Therefore, it holds promise as a potential neurodiagnostic for young children. We set out to explore whether NIRS could be utilized in assessing the risk of developmental psychopathology in young children. A growing body of work indicates that temperament at young age is associated with vulnerability to psychopathology later on in life. In particular, it has been shown that low effortful control (EC), which includes the focusing and shifting of attention, inhibitory control, perceptual sensitivity, and a low threshold for pleasure, is linked to conditions such as anxiety, depression and attention deficit hyperactivity disorder (ADHD). Physiologically, EC has been linked to a control network spanning among other sites the prefrontal cortex. Several psychopathologies, such as depression and ADHD, have been shown to result in compromised small-world network properties. Therefore we set out to explore the relationship between EC and the small-world properties of PFC using NIRS. NIRS data were collected from 44 toddlers, ages 3–5, while watching naturalistic stimuli (movie clips). Derived complex network measures were then correlated to EC as derived from the Children's Behavior Questionnaire (CBQ). We found that reduced levels of EC were associated with compromised small-world properties of the prefrontal network. Our results suggest that the longitudinal NIRS studies of complex network properties in young children hold promise in furthering our understanding of developmental psychopathology.

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Introduction

Near-infrared spectroscopy

Near-infrared spectroscopy (NIRS) is an emerging functional neuroimaging technique, which allows non-invasive assessment of brain function via regional changes in blood flow and the concentration of oxygenated and deoxygenated hemoglobin (Oxy-Hb and Deoxy-Hb) by measuring the transmittance of near IR light at the scalp. It is generally assumed that an increase in regional brain activation is related to an increase in blood flow and/or local blood oxygenation.

Most functional neuroimaging studies have used functional magnetic resonance imaging (fMRI), which remains the gold standard due to its superior signal-to-noise ratio and spatial resolution. However, NIRS has important advantages relative to fMRI: NIRS is restraint-free and relatively robust with respect to head movement, making it attractive for use with young children. Also, NIRS has a good temporal resolution, typically 10 Hz compared to 0.3 Hz typical for fMRI. Finally, NIRS is comparatively inexpensive, and is portable, making it a practical assessment tool in many situations where fMRI is not. NIRS, like EEG, is limited by its ability to only measure from the surface of the brain; however, its advantages suggest that it may have significant potential as a diagnostic tool for psychiatric disorders for which cortical-limbic control is a biomarker (Radulescu et al., 2012; Tolkunov et al., 2010), and/or as a predictor of risk for their later development.

Several previous functional NIRS studies have reported significant differences in Oxy-Hb response to emotion-related stimuli in small samples of healthy participants (Herrmann et al., 2008; Marumo et al., 2009; Suzuki et al., 2005; Yang et al., 2007) and a number of studies have used functional NIRS in infants (Grossmann et al., 2008; Nakato et al., 2009, 2011; Wilcox et al., 2012). However, no previous study has investigated the relationships between the NIRS signal and risk for development of psychopathology within children. Thus the potential utility of NIRS as an indicator of risk for psychiatric disorder is unknown.

Temperament and risk for psychopathology

A growing body of work highlights associations with temperament as promising avenues for understanding vulnerability to psychopathology (Bijttebier and Roeyers, 2009). Several studies have shown that early age temperament can be linked to conditions such as anxiety, depression and attention deficit/hyperactivity disorder (ADHD) later on in life (Nigg, 2006). In particular, NIRS has important advantages relative to fMRI: NIRS is restaint-free and relatively robust with respect to head movement, making it attractive for use with young children. Also, NIRS has a good temporal resolution, typically 10 Hz compared to 0.3 Hz typical for fMRI. Finally, NIRS is comparatively inexpensive, and is portable, making it a practical assessment tool in many situations where fMRI is not. NIRS, like EEG, is limited by its ability to only measure from the surface of the brain; however, its advantages suggest that it may have significant potential as a diagnostic tool for psychiatric disorders for which cortical-limbic control is a biomarker (Radulescu et al., 2012; Tolkunov et al., 2010), and/or as a predictor of risk for their later development.

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Small-world network properties and psychopathology

Complex network analysis (CNA), an extension of graph theory, is used to explore both anatomical and functional connectivity in the brain. CNA quantifies the functional organization of a given network in terms of integration, segregation, centrality and resilience (Rubinov and Sporns, 2010). In particular, CNA assesses the small-world properties of networks; that is, the degree to which functional demands for integration and segregation are balanced. Importantly, small-world properties have been shown to be indicative of various abnormal states of the central nervous system such as ADHD (Wang et al., 2008), depression (J. Zhang et al., 2011), obsessive compulsive disorder (T. Zhang et al., 2011) and schizophrenia (Bassett et al., 2008; Liu et al., 2008).

While CNA has been applied mostly to fMRI, a recent study demonstrated the feasibility of application of CNA to whole brain resting state NIRS (Niu et al., 2012). In this study it was found that cortical functional connectivity exhibited small-world properties as could be expected from numerous fMRI studies.

Study design

Our aim was to investigate the potential of NIRS for assessing risk for psychopathology in young children. To do so we set out to explore the relationship between EC, a known predictor of child psychopathology and network small-world properties, which neuroimaging has linked to psychopathology prevalent in children. Accordingly, we imaged the prefrontal cortex, a prominent part of the brain network associated with EC, during passive viewing of movie clips that differed either in (a) their emotional content (and novelty) or (b) their novelty alone. Our choice of stimuli was grounded in our previous research on fMRI imaging of adults (Mujica-Parodi et al., 2009; Tolkunov et al., 2010), which confirmed that prefrontal regions provide the inhibitory component of the control circuit modulating emotional arousal—the dynamics of which are disrupted in trait anxiety. However, because the EC construct includes both emotional and attentional features, because prefrontal regions are also strongly associated with attention modulation, and because stimuli with greater emotional valence also tend to have increased novelty, we were careful to provide a design capable of controlling for attentional focus towards novelty alone. Doing so would permit us to identify whether disrupted dynamics associated with lowered EC were associated with the emotional components of EC, the attentional components of EC, neither, or both. This has important clinical implications in dissociating risk for illnesses that might be primarily emotional in nature (e.g., generalized anxiety disorder, major depressive disorder) versus those that might be primarily attentional in nature (e.g., attention deficit hyperactivity disorder), versus those that might include both strong emotional and attentional components (e.g., autism spectrum disorder).

From a control theory perspective, a well-regulated system is capable of efficient adaptation to outer perturbations (which in the case of brain circuits manifest as shift from baseline activity). In our experimental design the system was “perturbed” through exposure to video clips: naturalistic rich stimuli enabling to mimic real life complexity in a controlled laboratory setting, which have been
previously shown to modulate prefrontal activity (Aalto et al., 2002; Goldberg et al., 2006). It was our expectation that the efficiency of frontal executive networks would manifest through maintaining an efficient dynamical regime, that is, network dynamics exhibiting small-world properties. As reduced effortful control indicates maladaptivity of executive brain function, we hypothesized that in our subjects reduced prefrontal network efficiency would be correlated with its behavioral counterpart, reduced effortful control, that is, that low levels EC would be associated with compromised small-world network properties in the prefrontal network as seen by NIRS.

Methods

Participants

Forty-four healthy children, between the ages of three and five, participated in the experiments. Data from nine children were excluded due to excessive motion artifact, or failure to comply with the experiment, leaving 35 children whose data were included in the analysis (18 males and 17 females, mean age of 4.5 years). This exclusion rate is consistent with that reported by previous NIRS studies of young children (Nakato et al., 2009, 2011; Otsuka et al., 2007). For all children, parents reported that the children had no significant impairment of vision, hearing, neurological illness or developmental delay. The Stony Brook University Institutional Review Board approved this study; informed consent was provided by parents of all children who participated.

Assessment of effortful control

EC was assessed using the Children’s Behavior Questionnaire (CBQ, Rothbart et al., 2001) – one of the most frequently used measures of child temperament in young children. The CBQ is a detailed assessment filled out by parents and yields scores for fifteen behavioral measures: Activity Level, Anger/Frustration, Attentional Focusing, Discomfort, Fear, High Intensity Pleasure, Impulsivity, Inhibitory Control, Low Intensity Pleasure, Perceptual Sensitivity, Positive Anticipation, Sadness, Shyness, Smiling/Laughter and Soothability. The CBQ is reported to have good convergent validity, good good convergence between the ratings of mothers and fathers, as well as adequate internal consistency within children in the age range we tested (Rothbart et al., 2001). Factor analyses show that scale scores coalesce into three factors: negative affectivity, extraversion/urgency, and effortful control. Following Rothbart et al. (2001), test scores were combined to produce EC scores: First, the reported loadings for each of the 15 scales for three year olds and four and five year olds were averaged to reflect the mean age of our sample. Next, the average coefficients were used to derive a weighted sum of the test scores.

Stimuli

NIRS recording was conducted as the participants watched the experimental stimuli. First, a small white fixation cross on a black background was presented for 10 s. The participants then passively viewed the stimuli, presented for 730 s. The stimuli were color clips of moving images, taken either from G-rated movies or from computer screen-savers, selected to provide unfamiliar, visually engaging non-human/non-animal stimuli.

The experiments were designed to dissociate response to novelty versus emotional content. Accordingly, two sets of stimuli, addressing each type of response, were presented in a single session using a 20 s block design (see Supplementary Fig. 1):

Experiment 1 (novelty)

1. Novel stimuli: seven different 20 s movie clips obtained from computer screen-savers, selected to provide unfamiliar, visually engaging non-human/non-animal stimuli.

2. Familiar stimuli: one of the set of 20 s movie clips obtained from computer screen-savers, which was presented repeatedly during each block in order to provide the equivalently visually engaging non-human/non-animal stimuli, but without any novelty.

Experiment 2 (emotional content)

1. Emotional stimuli: seven different 20 s children’s G-rated cartoon movie clips, selected to elicit emotional responses (dramatic scenes involving fight or flight).

2. Neutral stimuli: seven different 20 s children’s G-rated cartoon movie clips, selected to elicit non-emotional responses (moving landscapes and non-emotional interactions between humans or animals).

The clips for both experiments were presented together, twice each, for 10 s each in a pseudorandom order, fixed over all participants. Between clips a fixation cross was displayed for 10 s. The stimuli were presented on a 20” LCD monitor at approximately 20° and approximately 60 cm away. During the experiments, participants were supervised by both an experimenter and a caregiver.

NIRS data acquisition

NIRS probes (Hitachi Medico, Kashiwa, Japan) were positioned on the head of each child by two experimenters. The positions of the placed optodes were measured using a Polhemus ISOTRAK II (Initin, London) magnetic tracker, controlled by a Hitachi ETG 4000 in the 18 detectors (24 channels) configuration. Five 10–20 markers (Jasper, 1958) were measured to allow offline registration to MNI coordinates: Nz (nasion), Iz (inion), AR (right ear), AL (left ear), and Cz (midpoint of the crown of the head). The ETG-4000 system was also used to measure the changes in concentrations of oxyhemoglobin (Oxy-Hb) and deoxyhemoglobin (Deoxy-Hb). We recorded from 24 channels with a sampling frequency of 10 Hz. Twelve channels (pairs of emitting and detecting fibers) were sampled from the right prefrontal cortex and the other twelve channels recorded from the left (Fig. 1). Two wavelengths of near-infrared light (695 and 830 nm) were projected through the skull. The intensity of the NIRS light illumination at each channel was 0.6 mW. The NIRS probes (Hitachi Medical) comprised 3 × 3 arrays with nine optical fibers: five emitters and four detectors. The optical fibers were held in place with a silicon holder. The emitters and detectors were separated by 2 cm. The probes were positioned at the location of the left and right prefrontal cortices (see Fig. 1). A headband was used to promote contact between the fibers and the scalp; where this could not be achieved, channels were rejected from the analysis.

Eye movement data

Eye movement was recorded using an EyeLink 1000 remote eye tracker (SR Research Ltd., Mississauga, Ontario, Canada), with high spatial resolution and a sampling rate of 500 Hz. For all subjects, viewing was binocular, but only the right eye was monitored. To evaluate eye movement behavior, x and y coordinate data were divided into stimulus and fixation intervals and then binned to a 1024 × 768 grid across subjects. The resulting data were normalized to unit sum to approximate the probability of gaze placement as a function of space.

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Optical data analysis

Data were first corrected for motion artifacts using the method of Cui et al. (2010). In this method Deoxy-Hb data is used to estimate movement in Oxy-Hb data through decorrelation. This results in corrected time series, which we will denote Oxy*-Hb. These data were corrected for residual motion artifacts as well as cardiac artifacts using NAP (Fekete et al., 2011a). To allow localization of the signal the recorded optode positions were projected onto the cortical surface and transformed into MNI coordinates using the method of Fekete et al. (2011b), which is implemented in NAP. The average optode positions across all participants are shown in Fig. 1.

To examine the effect of the potential confound of participant motion on our results, we computed three measures of motion artifacts of the NIRS data. The first measure was the mean differences of the final preprocessed time series from the raw time series, averaged across all 24 channels. The second measure was the mean standard deviations of the raw data, averaged across all 24 channels. The third measure was the difference between the mean standard deviations (averaged across all 24 channels) of the raw data and the preprocessed data. These three measures of motion were highly correlated (p < 0.001). We examined correlations between these measures of motion artifacts and subscales of the CBQ and found no significant correlations.

Condition-based GLM analysis

Activation for each subject was inferred using NAP. Oxy*-Hb data were fit with a FIR model comprising 20 s long basis functions. To correct for autocorrelations, data were whitened according to a power-law, and pre-whitened with a high-pass filter of 0.01 Hz. The estimated GLM coefficients and variances were used for the group analysis following Beckmann et al. (2003) to infer the novel/familiar and fearful/neutral contrasts.

Assessing network small-world properties

To derive complex network measures, first the inter optode correlation matrix was computed for the entire time series filtered between 0.007 and 0.06 Hz (Achard et al., 2006) to overcome drift and non-physiological noise (Niu et al., 2012), setting negative and autocorrelations to zero. Next the resulting connectivity matrix was thresholded to retain only a fraction of the strongest connections (5%–95% in 5% increments), after which the resulting connectivity patterns were transformed to binary format. Next we computed the following global CNA measures: characteristic path length (Watts and Strogatz, 1998), a measure of network segregation, and the small-world index (Humphries and Gurney, 2008), which measure the balance between network integration and segregation relative to comparable random networks (see Appendix A for exact definitions). Additionally, we computed three per node measures: node betweenness centrality (Freeman, 1979), node degree (the sum of edges), and node efficiency (Latora and Marchiori, 2001).

Results

Eye movement analysis

We were able to collect adequate eye movement data for 28 of the 35 participants whose NIRS data met inclusion criteria. To assess the extent to which the children complied with task demands, we computed the group-wise co-occurrence empirical probability distribution for the stimulus and fixation parts of the task separately. As can be seen in Supplementary Fig. 2, on average subject gaze was focused mostly on the central part of the screen, indicating the subjects were compliant in viewing stimuli.

Prefrontal deactivation during engaging movie viewing

The temporal profile of the Oxy*-Hb response to the task design and different conditions is presented in Fig. 2. In general, movie clips resulted in prefrontal deactivation. We conducted one-sample F-tests for prefrontal Oxy*-Hb concentrations to examine differences in activity for the novel/familiar conditions and the emotional/neutral conditions. Using a multiple-comparisons-corrected threshold of \( p = 0.002 \) (0.05 / 24), we found significantly decreased Oxy*-Hb response for novel, as compared to familiar, clips (Fig. 3) as well as for emotional, as compared to neutral, clips (Fig. 4). The waveforms across channels for both contrasts are depicted in Supplementary Fig. 3.

Small-world properties of prefrontal cortex

The group wise correlation profile for the Oxy*-Hb data is shown in Supplementary Fig. 4. As was found in a previous NIRS study for the entire cortex (Niu et al., 2012), the prefrontal network exhibited small-world properties. First, increased functional integration was indicated by reduced characteristic path length as compared to matched random networks. Similarly, we observed increased functional segregation indicated by an increased clustering coefficient as compared to matched random networks. Finally, in accordance with the above results, an increased small-world ratio was observed as well (Fig. 5). This was true for all connectivity thresholds employed
in this study, and the behavior of these parameters as a function of sparseness was highly similar to network properties previously reported (Niu et al., 2012) in the whole brain.

Relationship between prefrontal small-world properties and effortful control

We computed the partial correlation between the derived network measures and EC, controlling for age, sex, and the motion artifact parameters described above. One-sided significance was corrected for multiple comparisons across threshold values, following the method of Benjamini and Hochberg (1995). EC and characteristic path length were negatively correlated (Fig. 6). Because lower scores indicate a high degree of integration, our result suggests that lower EC was associated with reduced prefrontal network integration. Similarly, we found that EC positively correlated with the clustering coefficient (Fig. 6, middle), such that reduced EC was associated with a decrease in frontal network segregation. Finally, EC was positively correlated with prefrontal small-worldness (Fig. 6, bottom). That is, reduced EC was associated with compromised efficiency in prefrontal networks.

As we employed the method of Cui et al. (2010) to clean Oxy-Hb data from gross movement artifacts, it was not possible to carry out similar analysis on the Deoxy-Hb data: the corrected decorrelated Oxy*-Hb data is a weighted sum of both types of data. We did however carry out the same analyses on Total-Hb data and obtained equivalent, although somewhat weaker, results (see Supplementary Fig. 5).

Fig. 2. Task related prefrontal deactivation. Top: The Oxy*-Hb time course averaged across subjects and channels. Shaded gray marks the standard error. Block markers are coded according to movie clip type. Bottom: The group average response to each of the four experimental conditions. Note the mirror symmetry in waveforms along the midline.

Fig. 3. Left: The time-course of the difference in Oxy*-Hb between the novel and familiar conditions for channel 22, averaged across subjects. The zero on the horizontal axis represents the beginning of the test phase and 20 (seconds) represents the end of the test phase. Right: Prefrontal regions showing significant differences in activation between the novel and familiar conditions.

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To see whether specific parts of the prefrontal network were instrumental in leading to the observed global properties of the prefrontal network we carried out local CNA on the Oxy*-Hb data. Analysis was carried out at a connection threshold of 0.5 in which the correlation between EC and the small-world index peaked (Fig. 6). We did not find significant differences in either node degree or efficiency. We did however find differences in betweenness-centrality (Supplementary Fig. 6).

Discussion

In this study, we monitored prefrontal activity in 35 young children through NIRS, during passive viewing of movie clips. Our goal was to link an aspect of temperament, effortful control (EC, Rothbart, 1989), which has been associated with risk for psychopathology later on in life (Nigg, 2006), with small-world properties of the prefrontal network, which have been linked to psychopathology in both children and adults (Rubinov and Sporns, 2010). The results of this analysis confirmed our hypothesis, that reduced EC is associated with compromised small-world network properties in prefrontal cortex, and were consistent with results of previous studies. Prefrontal networks exhibited less functional integration in children with low levels of EC. Similarly, low EC was associated with lower levels of functional segregation. Moreover, low EC was associated with reduced levels of the small-world index. The latter is commonly interpreted as attesting to reduced functional efficiency of cortical networks, as has been corroborated by patient studies, in which compromised small-world properties were

Fig. 4. Left: The time-course of the difference in Oxy*-Hb between the emotional and neutral conditions for channel 9, averaged over all trials. The zero on the horizontal axis represents the beginning of the test phase and 20 (seconds) represents the end of the test phase. Right: Prefrontal regions showing significant differences in activation between the emotional and neutral conditions.

Fig. 5. Small-world properties of the prefrontal network. Prefrontal functional connectivity during the task exhibited robust strong world properties across the entire possible range of connectivity thresholds (sparseness). Top right: The clustering coefficient, and the inverse of the characteristic path length were computed as a function of connection threshold (sparseness), and normalized to the respective values derived from random networks. The normalized measures were multiplied to derive the index. Bottom left: Zoom in on connection threshold values greater than 20%.

found in patient populations either globally, or in brain networks pertaining to the underlying condition (Bassett et al., 2008; Liu et al., 2008; Wang et al., 2008; J. Zhang et al., 2011; T. Zhang et al., 2011). In our study, the prefrontal cortex was deactivated in response to engaging stimuli, and therefore indicates a global measure of attention that was non-specific to either novelty or emotional content. This was expected on the basis of previous studies, in which viewing of engaging movie stimuli also resulted in prefrontal deactivation (Aalto et al., 2002; Goldberg et al., 2006). This indicated the potential suitability of the chosen paradigm for the purposes of the study—given that the stimuli required focused attention and manipulated either emotion or level of arousal, and indeed modulated activity in the imaged cortical regions. There have been recent concerns regarding the impact of local skin blood flow changes on signals obtained by NIRS sensors, especially when placed on the forehead (Takahashi et al., 2011).

Fig. 6. Correlation between effortful control (EC) and prefrontal network small-world properties. Partial correlations controlling for age, sex and motion artifact were derived between the composite score and global complex network measures. Binary network representations were derived from inter-optode correlations after applying threshold values ranging from 0.05 (the top 5% of correlation values) to 0.95. These binary patterns were used to compute CNA measures. Left — partial correlation significance as a function of connectivity threshold. One sided significance was corrected for multiple comparisons following the method Benjamini and Hochberg (1995). Right — the scatter plots of partialled values (both CNA measures and EC scores), as well as the result of a linear fit of EC scores to CNA measures resulting from the threshold values yielding maximal correlation. Top: correlation between EC and characteristic path length—a measure of functional integration. Middle: correlation between EC and the clustering coefficient—a measure of functional segregation. Bottom: correlation between EC and the small-world index, a measure of the balance between functional integration and segregation.

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several indications suggest that our results derive from underlying cortical signals. First, the prefrontal network exhibited small-world organization that was virtually identical to that found through whole brain analysis using NIRS (Niu et al., 2012). These global functional invariants by nature attest against the notion of underlying local contained causes. Second, the functional correlations at the root of our CNA analyses exhibited clear bilateral effects. This can be seen by the mirror symmetry along the medial longitudinal fissure in evoked responses for all conditions (Fig. 2, bottom). Similarly, the group-wise pattern of correlation for Oxym−Hb showed marked bilateral effects (Supplementary Fig. 4 bottom); for example, correlations in the furthest bilaterally corresponding cortical sites were nearly as strong as local correlations and exceeded midrange correlations in magnitude. Finally, channels 11, 12, 23 and 24 (see Fig. 1) exhibited reduced mid- and long-range functional correlations (Supplementary Fig. 4 — middle). These channels were obtained from optodes placed directly above the brows, that were not optimally positioned to read out cortical signals as on average they projected virtually onto the ventral edge of the brain (Fig. 1). Hence, it is possible that these optodes, and hence channels, suffered from signal loss, explaining the observed weakened network wide functional coupling to these loci. Yet, at the same time these optodes were in contact with the skin, hence were in a position to detect local blood flow signals, just as any of the other optodes. In other words, in this case there was a clear indication to the predominant cortical source underlying our results. An obvious limitation of our study is that prefrontal network properties were not linked to psychopathology directly, but only to a known risk factor. Clearly, much more additional work is necessary to validate the approach we present here. Nevertheless, our results do suggest a link between developmental psychopathology and prefrontal network properties, suggesting that these could potentially pave the way for future NIRS-based diagnostics in children.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2013.07.022.

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Conflict of interest

None.

Appendix A. Complex network measures

Basic definitions

Let \( N = \{1, 2, \ldots, n\} \) be the set of all nodes in the graph, and \( v_{ij} \) the weight of the edge connecting nodes \( i \) and \( j \). The degree of node \( i \) is \( k_i = \sum v_{ij} \). The shortest path distance is: \( d_{ij} = \sum f(\sum v_{ijk}) \) where \( g_{ij} \) is the shortest path between \( i \) and \( j \), and \( f \) is a map from weight to length (e.g., the reciprocal function for correlation matrices, where higher values indicate shorter effective distances; or the identity function in case of a binary graph).

Characteristic path length (Watts and Strogatz, 1998) of a graph is given by:
\[
L = \frac{1}{2} \sum_{i} L_i \quad \text{where} \quad L_i = \frac{1}{n_i} \sum_{j \neq i} d_{ij}
\]

Clustering coefficient (Watts and Strogatz, 1998) is:
\[
C = \frac{1}{2} \sum_{i} C_i \quad \text{where} \quad C_i = \frac{1}{2} \left[ \sum_{j \neq i} \frac{2}{v_{ij}(v_{ij} - 1)} \right].
\]

Small-worldness (Humphries and Gurney, 2008): first the ratio between the clustering coefficient and characteristic path length \( S \) is computed. Next, the respective quantities \( C \) and \( L \) are computed for random graphs arising from permuting the original connectivity patterns. Finally, the small-world index is given by the ratio between \( S \) and \( S_r \).

Node efficiency (Latora and Marchiori, 2001) of a graph:
\[
E_i = \frac{\sum_{j \neq i} v_{ij} d_{ij}(N_i)^{-1}}{n(n-1)}
\]

where \( d_{ij}(N) \) is the length of the shortest path between \( i \) and \( j \), which contains only neighbors of \( i \).

Node betweenness centrality (Freeman, 1979):
\[
b_i = \frac{1}{(n-1)(n-2)} \sum_{j \neq i} \sum_{k \neq i, j} \frac{d_{jk}(i)}{d_{jk}}
\]

where \( d_{jk}(i) \) is the number of shortest paths between \( j \) and \( k \) that pass through \( i \).

References


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