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Letter to the Editor

Edge vulnerability in neural and metabolic networks

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Abstract. Biological networks, such as cellular metabolic pathways or networks of corticocortical connections in the brain, are intricately organized, yet remarkably robust toward structural damage. Whereas many studies have investigated specific aspects of robustness, such as molecular mechanisms of repair, this article focuses more generally on how local structural features in networks may give rise to their global stability. In many networks the failure of single connections may be more likely than the extinction of entire nodes, yet no analysis of edge importance (edge vulnerability) has been provided so far for biological networks. We tested several measures for identifying vulnerable edges and compared their prediction performance in biological and artificial networks. Among the tested measures, edge frequency in all shortest paths of a network yielded a particularly high correlation with vulnerability and identified intercluster connections in biological but not in random and scale-free benchmark networks. We discuss different local and global network patterns and the edge vulnerability resulting from them.

Keywords: Network vulnerability – Brain networks – Small world – Cluster – Edge betweenness

1 Introduction

Extensive evidence shows that biological networks are remarkably robust against damage of their nodes as well as links among the nodes. For example, Parkinson's disease only becomes apparent after a large proportion of pigmented cells in the substantia nigra are eliminated (Damier et al. 1999), and in spinal cord injuries in rats, as little as 5% of the remaining cells allow functional recovery (You et al. 2003). Many metabolic networks, as well, were found to be robust against the knockout of single genes. This feature is both due to the existence of duplicate genes as well as alternative pathways that ensure that a certain metabolite can still be produced using the undamaged parts of the network (Wagner 2000).

Approaches to network analysis have been used to investigate various types of real-world networks in which persons, proteins, brain areas, or cities are considered nodes and functional interactions or structural connections are represented as edges of the network (Strogatz 2001). Many such systems display properties of small-world networks (Watts and Strogatz 1998), with clustered local neighborhoods and short characteristic paths (or average shortest paths, ASP). Also, some networks possess more highly connected nodes, or hubs, than same-size random networks, leading to a power-law degree (*scale-free*) distribution of edges per node, where the probability for a node possessing k edges follows $k^{-\gamma}$ (Barabási and Albert 1999). Such scale-free networks are error-tolerant toward random elimination of nodes but react critically to the targeted elimination of highly connected nodes (Albert et al. 2000). It has been shown that cerebral cortical networks in the cat and macaque monkey brain display a similar behavior (Martin et al. 2001). While networks may possess features of both small-world and scale-free organization, the two topologies are not necessarily identical.

Whereas previous studies explored the impact of lesioning network nodes (Barabási and Albert 1999), the effect of *edge* elimination in biological networks has not yet been investigated. How can edges that are integral for the stability and function of a network be identified? In some systems, for instance transportation or information networks, functional measures for the importance of edges, such as flow or capacity, are available. For many biological networks, however, such measures do not exist. In brain connection networks, for example, a projection between two regions may have been reported, but its structural and functional strength is frequently unknown or not reliably specified (Felleman and van Essen 1991), and its functional capacity may vary depending on the task (Büchel and Friston 1997). Similarly, in biochemical networks, reaction kinetics are often highly variable, or generally unknown (Schuster and Hilgetag 1994; Stelling et al. 2002). However, the analysis of a network's structural organization

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may already provide useful information on the importance of individual nodes and connections, by identifying local features and investigating their importance for global network structure and function. Specifically, we are interested in these questions: Which structural patterns can be identified in a network? Do biological networks have specific features compared to artificial networks? As examples of biological networks we analyzed cortical fiber networks, metabolic networks, and protein interaction networks, as well as, for comparison, an artificial network, the German highway system.

In our analyses we tested the effect of eliminating single edges from networks. For some of the studied networks, such as cortical connectivity, structural damage might also result in multiple lesions of connections or regions. Such lesions can lead to network fragmentation and may be theoretically analyzed within the framework of edge or vertex cut sets (Sporns 2002). A computational algorithm to predict the effect of multiple network perturbations (or lesions) was presented as part of the MSA (Multi-perturbation Shapley value Analysis) approach (Keinan et al. 2004). In the present article, however, we focus on the impact of eliminating single edges to infer network patterns and their vulnerability.

Two established parameters for characterizing networks are the average shortest path (ASP) and the clustering coefficient (CC). The ASP is the average number of edges that have to be crossed in order to reach one node from another. For a network with N nodes, it is calculated as the average of all existing shortest paths:

$$ASP = \overline{d(i,j)} \quad \text{with} \quad i \neq j \quad \text{and} \quad d(i,j) \neq \infty \,, \qquad (1)$$

where $d(i, j)$ is the number of edges of the shortest path between nodes i and j. Infinite distances between unconnected nodes, which occur after network fragmentation, are excluded from the average calculation. We used the deviation of the ASP before and after edge elimination as a measure of network damage.

The clustering coefficient of a node v with k_v adjacent nodes (neighbors) is defined as the number of edges existing among the neighbors divided by the number $k_v^2 - k_v$ of all possible edges among the neighbors (Watts 1999). We use the term clustering coefficient as the average CC for all nodes of a network. Networks with an ASP comparable to randomly connected networks but with much higher CCs are called *small-world* networks (Watts and Strogatz 1998). These systems exhibit network clusters that are regions in which many interconnections exist within a cluster but only few connections run between clusters. Various kinds of networks, such as electric power grids and social networks, display small-world properties (Watts and Strogatz 1998). In addition, neural networks of *C. elegans* and cortical networks of the cat and macaque were also shown to be small-world networks (Watts and Strogatz 1998; Hilgetag et al. 2000; Sporns et al. 2000) and to exhibit a clustered architecture (Hilgetag et al. 2000).

2 Materials and methods

2.1 Investigated biological and artificial networks

2.1.1 Brain networks We investigated long-range fiber projections in the cat and macaque brain. Nodes were brain regions or areas (e.g., V1), and edges were fiber connections between them. We considered connectivity data for a nonhuman primate, the macaque monkey (73 nodes; 835 edges; density 16%), and the cat (55 nodes; 891 edges; density 30%) (Scannell et al. 1995, 1999; Young 1993). In both species, the data included connections between cortical regions, as well as a few subcortical structures (e.g., the amygdala) and regions of entorhinal cortex. These networks possess properties of small-world networks (Hilgetag et al. 2000) and also show a similar response to attack as scale-free networks (Martin et al. 2001). The CC of these networks ranged between 40 and 50% (cf. Table 1).

2.1.2 Protein–protein interactions As an example of biochemical networks, we examined the protein–protein interactions of the *S. cerevisiae* yeast proteome (Jeong et al. 2001). The data consisted of 1,846 proteins and 2,203 distinct functional relationships among them, forming 4,406 unidirectional edges in the network graph (data from http://www.nd.edu/~networks/database/). With a value of 6.8%, the clustering coefficient was considerably smaller than for brain networks. As a further difference, the protein interactions network consisted of 149 disconnected components. The main component contained 79% of the proteins, and the remaining components mostly were composed of only one pair of proteins. As shown earlier (Jeong et al. 2001), connections in this network are also distributed in a scale-free fashion. However, the yeast two-hybrid method yielding protein interaction data (Ito et al. 2001; Gavin et al. 2002) produces many artifacts (Kitano 2003) that might have influenced prediction results.

2.1.3 Metabolic networks Cellular metabolic networks of different species were analyzed. Nodes here were metabolic substrates, and edges were considered as reactions (Ravasz et al. 2002) (data at http://www.nd.edu/~networks/database/). For bacteria, we investigated the metabolism of *E. coli* with 765 metabolites and 3,904 reactions. For eukaryotes, the data for *Arabidopsis thaliana* (299 metabolites and 1,276 reactions) and the yeast *S. cerevisiae* (551 metabolites and 2,789 reactions) were examined.

2.1.4 Transportation network Data for the German highway (Autobahn) system were explored as a comparative example of human-made transportation networks. The network consisted of 1,168 location nodes (that is, highway exits) and 2,486 road links between them (Autobahn-Informations-System, AIS, from http://www.bast.de). Only highways were included in the analysis, with smaller and local roads ("Bundesstrassen" and "Landstrassen") discarded. Parking and resting locations were also excluded from the set of nodes. Furthermore, multiple highway exits for the same city were merged to

Table 1. Density, clustering coefficient (CC), average shortest path ASP, and correlation coefficients r for different vulnerability predictors of the analyzed networks (the index refers to the number of nodes)

	Density	CC	ASP	r_{PD}	r_{DD}	r_{MI}	r_{EF}
Macaque_{73}	0.16	0.46	2.2	0.10^b	0.57^b	-0.40^b	0.84^b
Cat_{55}	0.30	0.55	1.8	0.08^a	0.48^b	-0.34^b	0.77^b
AT_{299} (metabolic)	0.014	0.16	3.5	0.04	0.09^b	-0.11^b	0.74^b
EC_{765} (metabolic)	0.0067	0.17	3.2	0.31^b	0.38^b	-0.15^b	0.75^b
SC_{551} (metabolic)	0.0092	0.18	3.3	0.11^b	0.22^b	−0.04	0.74^b
SC_{1846} (protein interactions)	0.0013	0.068	6.8	0.24^b	0.02	-0.14^b	0.60^b
German highway_{1168}	0.0018	0.0012	19.4	0.19^b	0.06^b	−0.04	0.63^b
Random_{73}	0.16	0.16	1.7	0.02	0.06	0.00	0.03
Scale-free_{73}	0.16	0.29	2.0	0.03	0.08	−0.01	0.03

[a] Significant Pearson Correlation, 2-tailed 0.05 level
[b] Significant Pearson Correlation, 2-tailed 0.01 level
Tested prediction measures were the product of degrees *PD*, absolute difference of degrees *DD*, matching index *MI*, and edge frequency *EF*

one location, representing the city as a single node of the network graph.

2.1.5 Benchmark networks Twenty random networks with 73 nodes and comparable density as the macaque network were generated. Moreover, 20 scale-free networks with 73 nodes and equivalent density were grown by preferential attachment (Barabási and Albert 1999), starting with an initial matrix of 10 nodes.

In addition to the random and scale-free networks, which consisted of only one cluster, networks with multiple clusters were considered. Twenty networks were generated with 72 nodes in order to yield three clusters of the same size with 24 nodes each. Connections within the clusters were distributed randomly, and six intercluster connections were defined to mutually connect all clusters. Average density of these networks was again similar to the macaque data.

2.2 Methods for detecting important connections

We tested four candidate measures for predicting vulnerable edges in networks. All algorithms were programmed in Matlab (Release 12, MathWorks, Inc., Natick, MA) as well as implemented in C for larger networks. Links were analyzed as directed connections for all networks.

First, the product of the degrees (PD) of adjacent nodes was calculated for each edge. A high PD indicates connections between two hubs that may represent potentially important network links.

Second, the absolute difference in the adjacent node degrees (DD) of all edges was inspected. A large DD signifies connections between hubs and more sparsely connected network regions that may be important for linking central with peripheral regions of a network.

Third, the matching index (MI) (Hilgetag et al. 2002) was calculated as the number of matching incoming and outgoing connections of the two nodes adjacent to an edge, divided by the total number of the nodes' connections [excluding direct connections between the nodes (Sporns 2002)]. A low MI identifies connections between very dissimilar network nodes that might represent important "shortcuts" between remote components of the network.

Finally, edge frequency (EF), a measure similar to "edge betweenness" (Girvan and Newman 2002; Holme et al. 2002), indicates how many times a particular edge appears in all-pairs shortest paths of the network. This measure focuses on connections that may have an impact on the characteristic path length by their presence in many individual shortest paths. We used a modified version of Floyd's algorithm (Cormen et al. 2001) to determine the set of all shortest paths and calculate the frequency of each edge in it. Multiple shortest paths between nodes i and j were present in the analyzed data sets. However, the standard algorithm only takes into account the first shortest path found. In order to account for edges in alternative shortest paths, the EF was calculated as the average of 50 node permutations in Floyd's algorithm. This led to an increased predictive value of this measure in all networks; however, the correlations already converged after ten permutations.

Another possible prediction measure, not used here, would be the range of an edge (Watts 1999; Sporns 2002), that is, the length of the shortest path between two adjacent nodes after the edge between them is removed. For dense networks, such as cortical connectivity, only range values of 2 and 3 occurred. Having only two classes of range values was not sufficient to distinguish vulnerable edges in detail. However, the range may be a useful predictor for sparse networks with higher ASP.

3 Results

3.1 Network patterns underlying edge vulnerability

The elimination of an edge from a network can have two possible effects on the ASP. First, the parts previously connected by this edge can still be reached by alternative pathways. If these are longer, the ASP will increase. Second, the eliminated edge may be a *cut-edge*, which means that its elimination will fragment the network into two

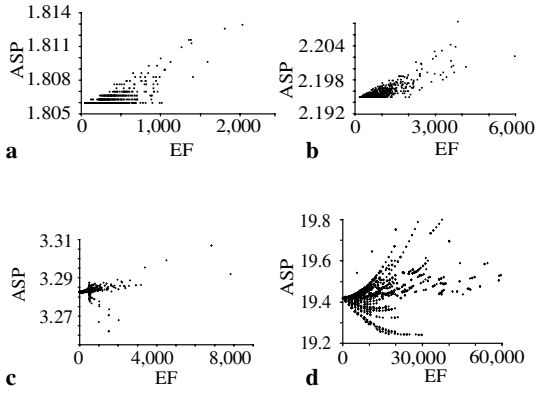

Fig. 1. Frequency of edges in the all-pairs shortest paths and resulting network damage after elimination. **a** Cat brain connectivity and primate (macaque) brain connectivity **b** show a strong correlation with damage. **c** Metabolic network of *S. cerevisiae*. **d** German highway system. Decreases of ASP were caused by eliminated cut-edges, leading to a separation of the network

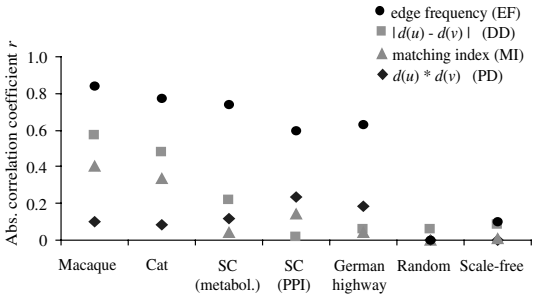

Fig. 2. Evaluation of the performance of four predictors for edge vulnerability. Note that the absolute correlation coefficient was used (MI would have had negative r). For all networks, except the random and scale-free benchmark networks, edge frequency had the highest correlation with edge vulnerability. In random networks and scale-free networks with only one cluster, however, the tested measures were unable to indicate impact of edge elimination

disconnected components. The probability for fragmentation, naturally, is larger in sparse networks. Network separation causes severe damage, as interactions between the previously connected parts of the network are no longer possible. Therefore, this impact can be seen as more devastating than the first effect, which may only impair the efficiency of network interactions. Our ASP calculation disregarded paths between disconnected nodes, which would be assigned an infinite distance in graph theory. Therefore, the ASP in disconnected networks was actually shorter, because paths were measured within the smaller separate components. Cut-edges, which lead to network fragmentation, frequently occurred in the highway network (30% of all edges) and the yeast protein interaction network (23% of all edges). However, cut-edges did not occur for cortical networks of cat and macaque and only to a limited extent ($< 5\%$ of all edges) in the studied metabolic networks.

In the present calculation both increase and decrease of ASP indicate an impairment of the network structure, and we took the deviation from the ASP of the intact network as a measure for damage. We evaluated the correlation between the size of the prediction measures and the damage (Table 1 for all networks). While most of the local measures exhibited good correlation with ASP impact in real-world networks, the highest correlation was consistently reached by the EF measure. For the cortical networks, the measures of matching index and difference of degrees also show a high correlation.

Cortical connectivity differed from the other networks not only in the performance of different edge vulnerability predictors but also in the density of connections and the amount of clustering. The cortical networks showed a higher density than the biochemical metabolic and protein–protein interaction networks. Whereas the highway network showed similar density to the biochemical networks, its clustering coefficient was much lower because of the high proportion of linear paths in the highway network. The random and scale-free benchmark networks – designed to resemble size and edge density of the macaque cortical network – are presented at the end of the table.

Figure 1 shows the ASP after edge elimination plotted against edge frequency (EF). For cortical networks (1 a, b) no network fragmentation occurred, and only an increase in ASP became apparent. For metabolic networks, e.g., the network of *S. cerevisiae* (Fig. 1c), also a few cut-edges, lowering the ASP, were targeted. For the highway network containing linear chains of nodes (Fig. 1d), many cut-edges were observed. The elimination of these links, therefore, resulted in two disconnected compartments, each of which had shorter path lengths.

3.2 Comparison with benchmark networks

We also calculated the four predictive indices for scale-free and random benchmark networks with 73 nodes and a similar number of edges as the macaque cortical network. Our comparisons focused on this network because it showed the highest correlation between prediction measures and actual damage for all four measures. For the benchmark networks, however, all measures were poor predictors of network damage (Fig. 2). This is surprising because scale-free networks generated here by growth and preferential attachment appeared to differ in their structure from real scale-free networks. Analyzing data for one of these real networks, the Internet at the autonomous systems level, which was previously shown to be scale-free (Barabási and Albert 1999), we found that EF as a prediction measure also performed well in this case ($r = 0.62$, not shown). The difference between the real and simulated scale-free networks may result from the fact that scale-free networks generated by growth and preferential attachment did not possess multiple clusters. We therefore tested whether the lack of connections between clusters might be the reason for the low performance of EF in the scale-free benchmark networks. We generated an additional 20 test networks, each consisting of three randomly wired clusters and six fixed intercluster connections (Fig. 3a). The intercluster connections (light gray) occurred in many shortest paths (Fig. 3b), leading to an assignment of the highest EF value, as no alternative paths of the same length were

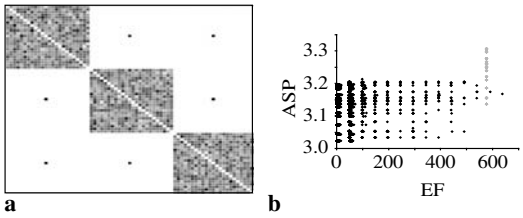

Fig. 3. Connectivity for multiclustered benchmark networks with comparable density to primate brain connectivity (cf. Sect. 2.1.5). The gray level of a connection in the adjacency matrix indicates relative frequency of an edge in 20 generated networks. *White* entries stand for edges absent in all networks. **a** Connectivity of test networks with three clusters and six predefined intercluster connections. **b** Edge frequencies in the all-pairs shortest paths against ASP after elimination of edges. *Light gray data points* represent the values for the intercluster connections in all 20 test networks. Intercluster connections not only have the largest edge frequency but also cause the most damage after elimination

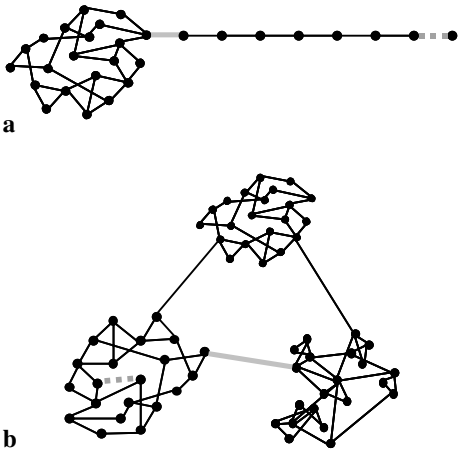

Fig. 4. Network pattern and corresponding edge vulnerability. **a** Elimination of edges of *linear chains of nodes* results in two disconnected components and a lower ASP. Edges eliminated at the proximal end of the chain (*solid line*) cause a larger change in ASP than at the terminal end (*dashed line*). **b** For *clustered networks*, edges within the clusters (*dashed line*) can be replaced by several alternative pathways. Therefore, their elimination causes a smaller increase of ASP than that of edges between clusters (*solid line*)

available. Furthermore, their elimination resulted in the greatest network damage, as shown by increased ASP.

3.3 Network patterns in biological networks

After establishing the high impact on ASP of edges with large EF, we investigated what made specific edges more vulnerable than others. We here discuss two patterns that occurred in many of the analyzed networks: first, linear chains of nodes that appeared in biological as well as the artificial (highway) networks, and second, clusters of highly interconnected regions of the network that occurred for all small-world networks, such as the analyzed cortical and biochemical systems.

Naturally, other and more complex network patterns are possible. We already discussed elimination of edges between a hub and a node with fewer connections (cf. Sect. 4.1). Also, the functional role of these patterns (e.g., feedback loops) is not examined here and merits further study.

3.3.1 Linear chains Linear chains of nodes with a terminal end (Fig. 4a) became apparent in various biological as well as artificial networks. These patterns were detected by testing for each node if it was part of a chain, that is, if it possessed two edges. In this case the chain was followed in both directions, and considered terminal, if at least one end of the chain had a terminal node. Using this method for identification, each terminal chain consisted of at least two edges. Nodes in the terminal chain were excluded from the further searching process. Terminal chains occurred frequently in the highway system but also arose in metabolic networks in the form of redox chain reactions. For the highway system, the average terminal chain length was 6.4 edges, with a maximum of 22 edges. For the yeast protein interaction network, 13% of the nodes were part of terminal chains, which were on average 2.25 edges long (maximum 6 edges). Eliminating edges at the terminal end of a chain would have a small impact, as only a few nodes become disconnected to the rest of the network. On the other hand, severing the first edge that connects a chain to the rest of the network eliminates all paths leading to the chain nodes from the shortest paths matrix. The effect of eliminating edges in a chain can be seen clearly for the highway network (Fig. 1d). Edges that connect chains to the rest of the network have a large EF, and their elimination greatly decreases ASP, in contrast to edges at the terminal end. Indeed, for networks that show many cut-edges, many terminal chains also occurred. For the highway system, 42% of all nodes were part of terminal chains. Similar properties of edge vulnerability arise when the terminal of a chain end is formed by a small subnetwork that is still smaller than the main network component at the start of the chain.

3.3.2 Clustered architecture A clustered or modular architecture is a characteristic feature of many naturally occurring networks, such as cortical connectivity networks in the primate (Young 1992, 1993; Hilgetag et al. 2000) or the cat brain (Scannell et al. 1995, 1999; Hilgetag et al. 2000) as well as metabolic networks (Ravasz et al. 2002). These systems are known to consist of several distinct, linked clusters with a higher frequency of connection within than between the clusters. Intercluster connections have also been considered important in the context of social contact networks, as "weak ties" between individuals (Granovetter 1973) and separators of communities (Girvan and Newman 2002). We therefore speculated that connections between clusters might be generally important for predicting vulnerability (Fig. 4b). Whereas many alternative pathways exist for edges within clusters, the alternative pathways for edges between clusters may be considerably longer. Interestingly, previously suggested growth mechanisms for scale-free networks, such as preferential attachment (Barabási and Albert 1999), or strategies for generating hierarchical networks (Barabási

et al. 2001) did not produce distributed, interlinked clusters. Consequently, the low predictive value of EF in the scale-free benchmark networks was attributable to the fact that scale-free networks grown by preferential attachment consisted of one central cluster but did not possess a multicluster organization. This suggests that alternative developmental models may be required to reproduce the specific organization of biological networks, and we have recently presented an algorithm based on spatial growth that can generate such distributed cluster systems (Kaiser and Hilgetag 2004).

4 Discussion

4.1 Measures for identifying vulnerable edges

We analyzed four measures for identifying vulnerable edges and predicting the impact of edge removal on global network integrity. Among these measures, the index of EF appeared consistently as the best predictor for damage to edges. The high performance of this measure may be linked to characteristic features of biological networks, as detailed below (Sect. 4.2). For the macaque monkey, seven out of the top ten connections with highest edge frequency originated from, or projected to, the amygdala. In addition, these edges were most vulnerable, as could be observed by the damage after edge elimination. Therefore, the amygdala appears to serve as a central link between many clusters of the network.

Following EF in terms of performance, the index for the difference of degrees also showed a high correlation in both the cortical and metabolic networks (Fig. 2). This means that connections between highly and sparsely connected nodes are vulnerable, especially in cortical networks. When a node with few connections is connected to an already well-connected node (hub), it can access a large part of the network by using routes involving the hub. After eliminating the connecting edge, the node would have to use longer alternative pathways to reach the same parts of the network. This effect is particularly strong if the node was the only one in its local neighborhood that was connected to the hub.

The matching index showed a large (negative) correlation with edge vulnerability in cortical networks and, to a lesser extent, the protein–protein interaction network. Therefore, edges between dissimilar connections, that is, with low MI, were more vulnerable. This was due to the cluster structure of these networks (cf. Sect. 4.2). Nodes with similar connectivity belong to the same cluster, and therefore multiple alternative pathways are available. Dissimilar nodes are more likely to be part of different clusters with few alternative pathways.

From theoretical studies it has been proposed for scale-free networks that edges between hubs are most vulnerable (Holme et al. 2002). However, in the networks analyzed here, both in the scale-free yeast protein interaction network as well as for cortical networks, edges that connected nodes possessing many connections (large product of degrees) were not particularly vulnerable. Although a low increase can be seen for the correlation coefficient, edges with maximum vulnerability occurred for a small product of degrees.

One of the general advantages of using prediction measures, instead of testing the damage for all edges of a network, is computational efficiency. For a network with e edges and n nodes, the order of time for the calculation of EF that can predict the effect of edge elimination for all edges is $O(n^3)$. This is lower than for testing the damage after edge elimination for all edges individually, calculating the ASP e times, resulting in a time complexity of $O(e \cdot n^3)$. The prediction measures presented here might therefore be particularly useful for large networks in which global testing is computationally impractical, or for networks with frequently changing connections demanding a regular update. Examples of these include acquaintance networks, Internet router tables, and traffic networks. Identifying vulnerable edges by EF generally appears to work well for various biological networks.

4.2 Vulnerable edges in biological networks

In the analyzed biological networks, intercluster projections may play an important role in linking functional units. For corticocortical networks, they connect and integrate different sensory modalities (e.g., visual, auditory) or functional subcomponents (Hilgetag et al. 2000). A lesion affecting these connections may result in dissociation disorders (Geschwind 1965).

For metabolic networks, reactions proceed more frequently within a reaction compartment (e.g., mitochondria and endoplasmatic reticulum) than between compartments. Therefore, in these systems as well, localized clusters arise, with many reactions within a compartment and few connections between compartments. Such an organization is also found in the investigation of protein–protein interactions and their spatial and functional clustering, in which fewer proteins from different groups interact (Schwikowski et al. 2000). Once again, interactions between proteins from different compartments correspond to intercluster connections and might thus be among the most vulnerable edges of the network.

To a lesser extent, "intercluster" connections also appeared in the highway network, as the highway subsystems of western and eastern Germany formed (spatially separate) dense regions connected by only four highways. That is, the elimination of four edges would once again split the German highway system into eastern and western components. Our analysis of artificial networks was restricted to networks without functional differentiation of edges or nodes. It remains to be seen if functional or social networks, for instance interactions of people with different functions within a company, may show a higher similarity in cluster architecture with biological networks.

Clustered network architecture appears to result in edge robustness in a similar way as scale-free architecture results in node robustness. Random elimination of edges will most frequently select edges within a cluster. For paths routed through these edges, various alternative pathways exist, and the damage after edge elimination is small. Targeted attacks on intercluster connections, on the other

hand, result in large network damage. We note that the cortical networks investigated here exhibit properties of both small-world (Hilgetag et al. 2000) and scale-free (Martin et al. 2001) networks and are therefore particularly robust to random failure of edges and nodes.

4.3 Conclusions

We examined how local network features and patterns relate to global network properties, such as robustness toward edge elimination. The correlation between different predictors and the actual damage after the elimination of a connection signified differences in the global network architecture. Specifically, various biological networks appear to be organized as distributed, linked network clusters. We have shown that intercluster connections represent the most vulnerable edges in these networks and that their position can be predicted using the edge frequency measure.

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